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ACUTE PERICARDITIS WITH SPECIAL REFERENCE TO CHANGES IN HEART SIZE*

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THE 5 cases that form the basis of this report have certain features in common. The patients were young or middle-aged men with normal hearts. During an acute respiratory infection, acute pericarditis supervened. The most remarkable feature was a rapid, conspicuous enlargement in the size of the heart, followed by a slower reversion toward normal and recovery without any demonstrable cardiac abnormality. Similar cases have been seen but are not included in this report, because in them the opportunity for x-ray confirmation of heart size was not available.

Of particular interest at the present time are 3 cases in which the pericarditis complicated atypical primary pneumonia.

CASE REPORTS

CASE 1. L. R., a 37-year-old, married man, with negative family and marital histories, entered the Beth Israel Hospital for the third time on September 19, 1929. The past history was negative except for thyrotoxicosis. During each of the previous two admissions (December, 1928, and March, 1929), subtotal thyroidectomy was performed for hyperthyroidism. The patient had had repeated paroxysms of auricular fibrillation, but there was no demonstrable structural abnormality of the heart by physical, roentgenographic or electrocardiographic examination. The blood pressure was normal. Following the second thyroidectomy he gained weight and felt well enough to return to work. However, the basal metabolic rate remained elevated, so that he was given Lugol's solution, and just prior to the third admission was subjected to three weekly roentgen-ray exposures over the thyroid gland, the basal metabolic rate being +18 per cent. The patient was readmitted several days after the onset of pain in the neck and across the upper chest, stiffness of all the muscles and general malaise. Examination on admission revealed slight injection of the pharynx, auricular fibrillation and fever.

The temperature varied between 98° and 102°F. until the 37th day after admission, remaining normal thereafter except as noted below. The pulse showed marked fluctuations, due to frequent short paroxysms of auricular fibrillation. The respirations averaged 20. During the febrile period general malaise, slight cough, a feeling of substernal constriction, sharp precordial pain and anorexia were the outstanding symptoms. The physical signs in the lungs were variable, consisting of slight dullness, diminished breath sounds and fremitus at the right base, crepitant rales under the angle of the right scapula, and a pleural friction rub in the right axilla. Examination of the heart on admission revealed no abnormalities, except in rhythm, but from the 22nd to 38th hospital days a pericardial friction rub was constantly audible over the entire precordium. It was not possible to demonstrate Ewart's sign, and distended neck veins, evidence of a congested

FIGURE 1.‡ *Case 1 (September 27, 1929).*

This film shows considerable enlargement of the heart shadow compared with that in a previous film. Normal cardiac landmarks are preserved.

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‡This and all subsequent figures are reproductions of x-ray films taken at a distance of seven feet. They were reproduced to show the cardiac outline as clearly as possible, without regard for the details of the pulmonary lesions.

liver, edema and blood pressure changes were not observed.

On the 57th day, the patient having recovered from the acute illness, thyroidectomy was performed for the third time. Convalescence was uneventful except for the recurrence of the precordial pain, the pericardial friction rub and a temperature of 102°F. on the 74th day. The patient was discharged in excellent condition 9 days later.

FIGURE 2. *Case 1 (December 10, 1929).*

The heart size is normal, and the configuration and measurements are identical with those in films taken prior to this patient's illness and subsequent to his recovery, a period of thirteen years.

The hemoglobin level and red-cell count were 85 per cent and 4,090,000, respectively. The white-cell counts varied between 6800 and 14,600 but were usually normal. Five vital-capacity determinations ranged between 2450 and 2800 cc. Teleroentgenographic measurements showed a total transverse diameter of 17 cm. on the 8th day (Fig. 1), and 14.2 cm. on the 82nd day (Fig. 2), the internal diameter of the chest being 28.5 cm. on both occasions. There was diminished radiance of both lung bases, especially on the right, and slight haziness in the right costophrenic angle. An electrocardiogram on admission showed auricular fibrillation and normal RST segments and T waves. Four days later, the RST segments were displaced upward in Leads 1 and 2, and the ascending limb of the T waves rose in a straight line; T_3 was inverted. All subsequent electrocardiograms displayed inverted T waves in all leads.

The patient developed diabetes in 1930, requiring insulin. Paroxysms of auricular fibrillation continued, but there was no demonstrable structural abnormality of the heart. Electrocardiograms and x-ray examinations were identical to those taken prior to the third hospital admission. He was last seen in 1942.

CASE 2. J. M., a 50-year-old pharmacist, entered the Beth Israel Hospital on January 29, 1941, and was discharged on February 12. His father died of cancer of the bowel, his mother of diabetes. Two sisters had diabetes, and four sisters and one brother were living and well. The marital and past histories were irrelevant.

The present illness began 12 days before entry with a feeling of malaise and feverishness. Finding his temperature elevated, the patient immediately went to bed. His physician found a few rales at both lung bases, a normal heart and a temperature of 100°F. Five days before entry, a pericardial friction rub was heard for the first time, and 2 days before entry the temperature rose to 102°F., after which it remained normal until entry. There was no chest pain at any time. The patient perspired a great deal and had an occasional dry cough. A diagnosis of bronchopneumonia was made.

The temperature on admission was 100.4°F. (rectal), rising to 101 on the 2nd day, after which it was normal. The pulse was 100 and respirations 22. The blood pressure was 120/80. A few fine crepitant rales were heard at both lung bases. A loud pericardial friction rub was audible all over the precordium, and persisted until January 30.

The hemoglobin level and red-cell count were normal. Three white-cell counts were 12,200, 7500 and 6600. A tuberculin skin test was positive in a dilution of 1:10,000.

FIGURE 3. *Case 2 (January 29, 1941).*

There is considerable cardiac enlargement, especially to the left. The silhouette is not suggestive of effusion, and the normal landmarks are preserved. The pulsations observed under fluoroscopic screen were of fair amplitude.

Sputum examinations for tubercle bacilli were negative. The corrected sedimentation rates were 2.3, 1.9, 1.1 and 0.7 mm.

A teleroentgenogram taken on the day of admission (Fig. 3) showed the total transverse diameter of the heart to be 15.8 cm. The roentgenologist reported the pulsations to be of fair quality, and there was no evidence of pericardial fluid. On February 10, the total transverse diameter of the heart was 13.5 cm. (Fig. 4).

Electrocardiograms showed the typical changes of acute fibrinous pericarditis; the last one, taken on February 11, still showed inverted T waves in Leads 2 and 3, but the T waves in Leads 1 and 4 had become upright. One month after discharge all leads were normal.

CASE 3. H. W., a 23-year-old man, was seen at home on July 29, 1933. He had never been robust, but led an active life and worked hard. Three years previously he had had a carbuncle on the upper lip. There was a history of diabetes in the mother and of rheumatic heart

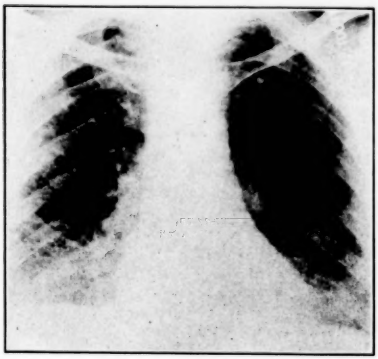

FIGURE 4. *Case 2 (February 10, 1941).*

The heart size is within normal limits. The silhouette corresponds to that seen in Figure 3.

disease in a brother. The present illness began 6 days before the first examination, with a slight unproductive cough and precordial pain. Three days later the patient felt chilly and the temperature rose to 101°F., reaching 102 on the following day. An insect bite above the right eye, sustained a week before, resulted in a purulent discharge, but this rapidly healed.

Examination showed consolidation of the left lower lobe. The heart and blood pressure were normal. On August 4, the signs were suggestive of fluid at the left base. From August 2 until admission to a hospital on August 8, a loud pericardial friction rub was constantly audible over the entire precordial area.

The white-cell count on admission was 25,400, falling gradually to 8700. X-ray examination of the chest disclosed fluid in the left pleural cavity, displacing the heart to the right.

A trocar thoracotomy was performed on the 2nd hospital day, and a free flow of pus was obtained. Culture yielded a pure growth of *Staphylococcus aureus.* The temperature fell sharply, but throughout the rest of the hospital stay there were slight rises above normal. X-ray films of the chest showed considerable improvement, and the patient was discharged on August 31, completely relieved except for slight pain in the left shoulder.

Two days later severe, sharp precordial pain recurred, followed in 2 or 3 days by sharp pain in both axillas, feverishness and profuse sweating. The patient remained up and about, but was readmitted 5 days following his discharge.

Examination revealed increased cardiac dullness, both to the right and to the left. The cardiac impulse was easily identified, and was not forceful but rather diffuse. The rate was rapid and the sounds were vigorous. There was a pleural friction rub at the left base. The abdomen was held tensely. The blood pressure was 120/70. The temperature fluctuated between 98 and 103°F. for the first 3 days, and was normal thereafter.

The white-cell count on admission was 19,800, rising to 23,800 on the following day, and thereafter quickly falling to a normal level. Two blood cultures were negative. Electrocardiograms revealed the classic pattern of early acute fibrinous pericarditis.

The roentgenologist's report is of particular interest. There was a remarkable change in the size of the heart in 9 days, with an increase of 2.4 cm. Pulsations of the heart were fairly distinct, but the shape of the heart was that of pericardial effusion. There was no evidence of undrained fluid in the left pleural cavity or new areas of dullness in either lung. The diaphragm moved fairly well on both sides.

Although there was no clinical evidence of pericardial effusion, several pericardial taps were attempted, yielding 1 cc. of sanguineous fluid, which proved negative on culture. By the 10th hospital day the heart size had returned to normal, and the patient was discharged. He has remained completely well to the present time.

CASE 4. S. B., a 30-year-old, married man, was seen in another hospital on September 19, 1942. The present ill-

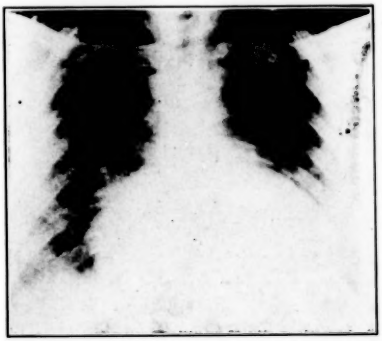

FIGURE 5. *Case 4 (September 19, 1942).*

The heart shadow is considerably enlarged, which is suggestive of pericardial effusion.

ness began on September 5 with headache, slight cough, profuse sweating, feverishness and generalized aching. When the patient was seen by his physician 5 days later the headache was still severe and the cough was unproductive and harassing. There were small pin-point areas of inflammation in the throat and crepitant rales in both lungs. The heart was normal. The patient was examined every day from then on, nothing unusual being found in the heart. On September 18 he felt well enough to shave himself. At 1:30 a.m. on the following day he was awakened by sharp precordial pain and a constricting pain in the anterior chest of great severity, requiring morphine. A pericardial friction rub was heard a few hours later. On arrival at the hospital an x-ray film was taken (Fig. 5), which showed considerable car

diac enlargement. The white-cell count was normal and the temperature was 101°F.

Physical examination showed a well-looking young man in no apparent discomfort, but complaining of occasional precordial pain. The area of cardiac dullness was increased. The palpable cardiac impulse was diffuse and corresponded with the left border of dullness. The rate was moderately rapid and the rhythm regular. A loud pericardial friction rub was audible over the entire precordial area. The heart sounds were distinctly and easily heard but were of rather poor quality. The only pulmonary finding was diminished respiratory excursion of the left lower chest. The blood pressure was 142/76. The pulse was of good quality; a paradoxical pulse could not be demonstrated. There was no distention of neck veins or liver, no Ewart sign and no edema or respiratory embarrassment.

Daily swings in temperature up to 104°F. were recorded until October 1, after which the temperature remained normal. The pulse averaged 85 and respirations

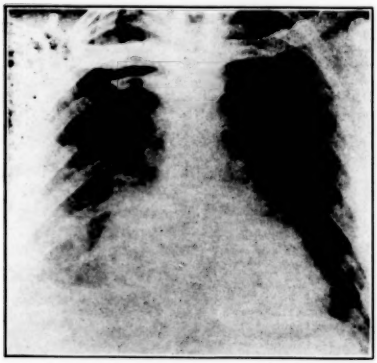

FIGURE 6. *Case 4 (October 2, 1942).*

There is still considerable enlargement of the heart shadow, but the landmarks are visible, and there is no suggestion of pericardial effusion.

20. Sulfadiazine was administered in adequate doses both before and after admission, but no benefit resulted and the drug was therefore discontinued. By September 22, the heart sounds had considerably improved, but the size of the heart was unchanged. The friction rub remained loud over the entire precordium until October 2, when it was limited to the region of the aortic valve. At that time the heart was much smaller (Fig. 6). An x-ray film taken on October 16 (Fig. 7) showed that the heart size was almost within normal limits. The blood pressure remained unaltered during the entire illness, and at no time were clinical signs of pericardial effusion elicited. Slight dullness and rales at both lung bases appeared, and finally a small area of bronchial breathing with increased spoken voice at the right base was detected. The cough gradually subsided, and the patient was well enough to leave the hospital on October 21. At no time was there dysphagia. Three weeks later there were no abnormal physical findings and the blood pressure was 142/90.

The white-cell count was normal except on September 20, when it reached 14,300, thereafter rapidly returning to normal. Several electrocardiograms showed the characteristic pattern of acute fibrinous pericarditis. An electrocardiogram on November 14 revealed entirely normal curves.

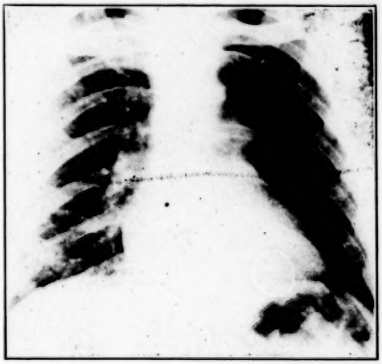

FIGURE 7. *Case 4 (October 16, 1942).*

The heart size is almost within normal limits. Comparison of the supracardiac shadow with that in Figure 5 shows an almost identical contour in both instances, indicating that, if fluid was present early in the course of the disease, the amount was very small.

CASE 5.* A. R., a 42-year-old, married salesman, entered the Beth Israel Hospital on August 21, 1942. The past history was negative except for tonsillectomy 25 years previously and influenza 24 years previously. The mother had hypertension.

The present illness began 2 weeks before admission with the onset of diarrhea, which lasted for 3 days. The patient continued to work as a traveling salesman, but 1 or 2 days after the diarrhea stopped he noted general malaise, loss of appetite and feverishness, and several days later a nonproductive cough. His physician made a diagnosis of "grippe" and advised rest in bed. The temperature fluctuated from normal to 103°F. up to the time of admission. The cough became progressively worse.

On August 21, the patient complained of stabbing precordial pain and sharp pain in the right anterior chest, aggravated by inspiration and causing some difficulty in breathing. He became aware of sudden rapid beating of the heart, together with great weakness. The family physician was unable to measure the blood pressure, and sent him to the hospital after administering morphine and Paredrine.

*Reported through the courtesy of Dr. Hyman Morrison.

Physical examination revealed a cold and clammy skin, respiratory difficulty owing to pleuritic pain, slight cyanosis and marked weakness. The temperature was 103°F. (rectal), the heart rate 214 (electrocardiogram), and the respirations 24. The posterior pharyngeal wall was in-

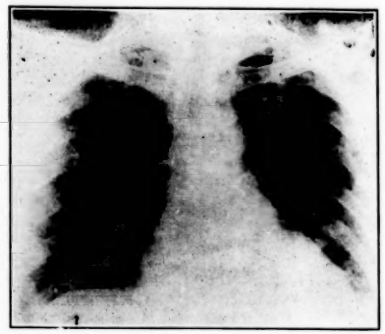

FIGURE 8. *Case 5 (August 26, 1942).*

There is considerable increase of the heart size. The normal landmarks are preserved, and there is nothing to suggest effusion.

jected. The heart appeared to be enlarged and extremely rapid and the sounds were of poor quality. There were scattered crepitant rales over both lung bases, but no areas of dullness and no bronchial breathing or other abnormal signs. The examination was otherwise negative.

The white-cell count on admission was 15,000, rising to 16,400 on the 4th hospital day and falling to 12,000 on the day of discharge. A heart film taken on August 26 (Fig. 8) showed enlargement of the heart and a pneumonic process at the right base.

The admission electrocardiogram showed a supraventricular type of tachycardia with a rate of 214. There was slight elevation of the RST segment in Leads 2, 3 and 4, without any displacement in Lead 1. The following day the rhythm was normal, and the rate 105; there was slight inversion of T_1, and the RST segments were still elevated in Leads 2, 3 and 4, with an upper concavity of the ascending limb of the T waves. The final electrocardiogram, taken the day before discharge, showed inverted T waves in all four leads.

Three tenths of a gram of quinidine hydrochloride was injected intramuscularly on admission, and 2½ hours later the heart rate was 100. The blood pressure was unobtainable at first, but rose slowly to 110/80 after the restoration of normal rhythm. Clinical improvement was rapid, in spite of the continuance of cough, but the rales at the bases increased, and slight dullness to percussion and suppressed breath sounds appeared over the right base. After the 3rd hospital day the temperature remained normal, and on the 8th day the patient insisted on going home.

He was next seen on December 5. Recovery was complete. The patient was working full time and attending gymnasium twice a week. Examination revealed no abnormalities of the heart or lungs, the electrocardiogram was of a normal pattern, and a teleroentgenogram (Fig. 9) showed the heart to be of normal size and the lung fields clear.

CAUSE OF THE CHANGES IN HEART SIZE

The differential diagnosis between dilatation of the heart and pericardial effusion is, as most clinicians agree, often a difficult and sometimes an insoluble problem. It is necessary to consider all the information obtained by examination of the heart and chest, a general and detailed study of the circulation, x-ray examination and fluoroscopy, electrocardiography and paracentesis. No one of these methods, including paracentesis, is infallible,

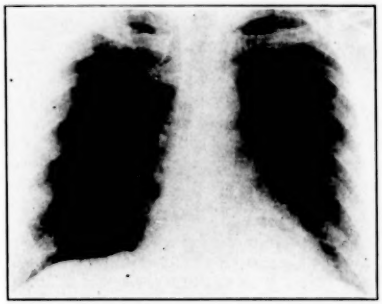

FIGURE 9. *Case 5 (December 5, 1942).*

This shows a normal cardiac silhouette. The general contour is similar to that in Figure 8.

but the collective data obtained by all of them may permit an accurate evaluation.

Nowadays, few clinicians cling to the idea that the presence of a pericardial friction rub is incompatible with an effusion in the pericardial sac. The location and distribution of the rub, however, is of some significance, since in most cases when excess fluid accumulates in the pericardial cavity the friction sound disappears in the region of the apex while persisting over the base of the heart and sternum.

The heart sounds are much more apt to be muffled, distant or absent in cases of effusion than in cases of dilatation, although in the latter the quality of the sounds may change and gallop rhythm may be present.

Increase in the area of absolute dullness on percussion may be striking in cases of pericardial effusion, and the abrupt transition from absolute dullness to normal resonance may help in the diagnosis. The area of supracardiac dullness may be increased.[1]

A paradoxical pulse is often found when fluid is present.

The cardiac impulse is usually absent when the pericardial sac contains a large amount of fluid, but is not obliterated in cases of cardiac dilatation. In the latter it may be noted as a diffuse, wavy impulse, and with few exceptions the left border of cardiac dullness corresponds to it. Should the cardiac impulse be detectable in a case of effusion, the left border of dullness may extend far to the left and below its location.

There has been considerable controversy regarding the presence and significance of physical signs over the posterior aspects of the lungs in pericardial effusion.[2] These signs include almost all those known to occur, but whether they correspond to those described by Bamberger–Ewart or present some less characteristic pattern, or are similar to the findings in pleural effusion, most observers agree that they are indicative of fluid in the pericardial cavity. Such signs may be elicited on the right as well as on the left side, or may be limited to the right side. In evaluating signs that are suggestive of pleural effusion, the latter may be excluded by x-ray examination. Posterior signs are never produced by heart enlargement alone.

Dilatation of the heart may occur without necessarily resulting in circulatory disturbances. It is well known, however, that pericardial effusion, even when not large, may cause profound alterations in the circulation. Dyspnea, cyanosis, markedly distended neck veins, a fall in arterial blood pressure with decreasing pulse pressure, a rise in venous pressure, an acutely distended and depressed liver and so forth are too well known to require comment. Yet in some cases large collections of fluid are compatible with an apparently normal circulation. The critical factor is the speed with which fluid accumulates in the pericardial sac.[3–6]

Reliance on x-ray examination in the differentiation of cardiac dilatation from pericardial effusion has been the cause of many errors in diagnosis. Nevertheless, this method of examination is of considerable value. The water-bottle configuration is not conclusive evidence of fluid and may be seen in cases of dilatation. The absence of pulsations on fluoroscopy may indicate fluid, but feeble pulsations may be misleading. Vigorous pulsation of the aortic knob and decreased pulsation of the left ventricular border suggest fluid (Freedman[7]). This author is also of the opinion that the most reliable diagnostic procedure is daily roentgen-ray examination of the heart. The finding of considerable change in its size within short periods of time he considers the best sign of fluid. A change in the outline of the cardiac silhouette with a change in position of the patient has been stressed by many observers.

Low voltage in the electrogram may be found when excess fluid is present.

The vital capacity is diminished with effusion.[3, 4]

The final proof of the existence of excess fluid depends on its actual demonstration by paracentesis, operation or autopsy. The failure to withdraw fluid with a needle does not prove its absence, for fluid may be encapsulated or the technic of paracentesis may be at fault.

The differential diagnosis between pericardial effusion and cardiac dilatation was carefully considered in each case in this series, and since the primary purpose of this paper is to report the rapid enlargement of the heart in acute fibrinous pericarditis, it will be necessary to state the reasons for considering the change in heart size as due to dilatation, and not to effusion in the pericardial cavity.

In Case 1, the first evidence of pericarditis was furnished by the electrocardiogram. The pattern observed was pathognomonic of early acute pericarditis, so that the diagnosis could be made with confidence in the absence of other evidence.[8, 9] Four days later a teleroentgenogram (Fig. 1) showed a great increase in the size of the heart compared to the previous plate, in which the measurements were within normal limits. The configuration of the heart shadow was not considered to be at all suggestive of effusion; the normal landmarks were preserved. An increase of such a magnitude in so short a time, if due to effusion, would in all probability have given rise to clinical manifestations of circulatory embarrassment. Yet these were singularly absent and the vital capacity was constant throughout the illness. The heart sounds remained normal; the friction rub, during the period of its audibility, could be heard at the apex, and there was a complete absence of characteristic posterior lung signs, distended neck veins, an enlarged tender liver, a change in blood pressure and so forth.

The diagnosis of pericarditis in Case 2 was first made on the basis of a friction rub. Five days later a teleroentgenogram (Fig. 3) showed considerable cardiac enlargement. The heart contour was not suggestive of fluid, and under the fluoroscope the cardiac pulsations were seen to be of fair amplitude. As in the previous case, there were none of the numerous signs or symptoms that are associated with a large or rapidly accumulating pericardial effusion. A second teleroentgenogram (Fig. 4), taken twelve days after the first one, showed the heart measurements to be within normal limits, and the total transverse diameter had decreased 2.3 cm.

In Case 3, the roentgenologist was so impressed by the remarkable increase in heart size in nine days that, although the cardiac pulsations were

distinct, it was his opinion that pericardial effusion was present. The electrocardiogram was pathognomonic of early acute fibrinous pericarditis. Clinically the heart was enlarged to the right and to the left. The cardiac impulse was easily felt and was not forceful but rather diffuse. The heart sounds were loud and there were no signs of compression. Nevertheless, in view of the recent empyema, the roentgenologist's opinion and the high white-cell count, several pericardial taps were attempted, but no fluid was found.

The cardiac silhouette in Case 4 suggested the presence of pericardial fluid. However, if it was present the amount was very small and was responsible for but little enlargement of the cardiac shadow. The teleroentgenogram taken several hours after the onset of pericarditis (Fig. 5) revealed a degree of enlargement that, if due entirely or for the most part to effusion, indicated an extremely rapid accumulation of fluid. This would in all probability have given rise to obvious circulatory disturbances. After seeing the x-ray film, every attempt was made to elicit clinical symptoms or signs of effusion, but these were consistently absent. The increase in cardiac dullness was inconspicuous, the apex impulse remained palpable, the friction rub was constantly audible over the apex of the heart as well as over the base, there was no change in cardiac outline with change of position, and the heart sounds were good. As the size of the heart decreased, even though there was still considerable enlargement, the contour no longer suggested the presence of fluid (Figs. 6 and 7).

The diagnosis of pericarditis in Case 5 was made solely on the basis of the electrocardiograms. The first two showed RST elevations without reciprocal depressions, and without changes in the QRS waves, which may be considered pathognomonic of early acute pericarditis. The third electrocardiogram showed inverted T waves in all the leads. The first x-ray film (Fig. 8) was taken five days after the onset of pericarditis and showed considerable enlargement of the heart without any of the features that are helpful in making a diagnosis of pericardial effusion. Clinically, as in the cases cited above, there was nothing to indicate a rapidly forming effusion.

In none of the cases was a decrease in amplitude of the QRS waves in the electrocardiogram, such as may be seen with pericardial effusion, observed.

The opinion appears warranted, in all these cases, that the rapid and striking increase in the size of the contents of the pericardial sac was due to an increase in the size of the heart itself and not to an increase of pericardial fluid. It is unlikely that fibrin deposits could have contributed materially to the rapid and striking changes in size that were seen. The same may be said in regard to swelling or edema or diffuse inflammatory infiltration of the heart muscle, particularly in view of the fact that circulatory efficiency did not appear to be impaired in the slightest degree. Simple dilatation of the heart, it would seem, was responsible for the phenomenon observed. Yet these patients appeared to be extremely well, and in none of them were symptoms or signs of circulatory disturbances observed.

Mechanism of Acute Dilatation

The anatomical structure of the pericardium and its ligaments[10] suggests that one of its functions is to restrain dilatation of the heart. Although there is no uniformity of opinion concerning this point, most of the clinical and experimental evidence favors this view.[11–26] If one were to ascribe the dilatation observed in our cases to pericarditis alone, it would be necessary to assume that the restraining function of the pericardium is lost when pericarditis occurs. There is no evidence to support this assumption; dilatation, moreover, does not occur in all cases of pericarditis. In suppurative pericarditis and in tuberculosis, a small heart is the rule. But in these two conditions an outpouring of fluid takes place that, together with the pericardium, which has yielded to the maximum extent conditioned by the inflammatory process and effusion, acts to restrain cardiac dilatation. It appears that in some cases, when the pericardium is inflamed, either effusion or cardiac dilatation follows.

It has been shown that, when the characteristic electrocardiographic pattern of acute pericarditis occurs, diffuse subepicardial myocarditis is present.[8, 9, 27–29] Since this pattern was observed in our cases, the additional factor of myocardial inflammation in causing dilatation must be considered.

Finally, the relatively slow heart rate, sinus arrhythmia and paroxysmal auricular fibrillation observed in our cases suggest that preponderant vagal tone may occur in the presence of pericardial inflammation and act as additional factors favoring cardiac dilatation. Van Liere and Crisler[26] have shown experimentally that vagal stimulation causes dilatation of the heart, and that the dilatation is greater, sometimes considerably so, if the pericardium is slit so that it loses its restraining function. Observations on the heart rhythm and electrocardiographic patterns following injection or removal of the stellate ganglions in dogs offer further suggestive evidence that the neurogenic mechanism may be disturbed following pericardial injury.[8]

The clinical evidence in the cases under discussion does not favor the view that impaired circulation in the pneumonic lung, anoxemia and toxemia were effective in producing cardiac dilatation.[30]

It is possible that paroxysmal tachycardia in Case 5 played some part in producing cardiac dilatation. It should be noted, however, that the paroxysm lasted only a few hours, and that the teleroentgenogram showing enlargement was taken five days after the paroxysm had ended. Cardiac dilatation does not often occur as a result of tachycardia, even with rates approaching 200,[31] and the available precise information[31-33] concerning the time of appearance of dilatation during paroxysmal tachycardia and its subsequent disappearance after the paroxysm has ended makes it extremely unlikely that the dilatation observed was related to the rapid heart action. Furthermore, in the accurately observed cases of dilatation associated with tachycardia, congestive failure was present; the cardiac silhouette, when the latter is present, may give a misleading impression of heart size.[34] These considerations make it even less likely that the paroxysms of auricular fibrillation had any bearing on the dilatation observed in Case 1.

Cardiac enlargement may occur in hyperthyroidism. In many if not all these cases, however, hypertension, coronary artery disease, valvular disease, congestive failure and so forth, are complicating factors.[35-37] For these reasons, as well as the mildness of the hyperthyroidism and reversion of the heart size toward normal before the hyperthyroidism was corrected, thyroid disease is excluded as the cause of dilatation in Case 1.

Discussion

Roentgenologic and orthodiagraphic demonstration of cardiac enlargement during acute infections has been reported by various observers.[30, 38, 39] A careful search of the literature failed to disclose similar studies showing cardiac enlargement in acute pericarditis, such as occurred in the cases here reported. Aside from its interest as a feature of pericarditis, the importance of not mistaking the heart enlargement for pericardial effusion is obvious, as emphasized by Barnes and Burchell[40]:

> I have seen many cases of pericarditis in which the heart became large very rapidly, and I am convinced that in some of these cases we are dealing with the finest examples of acute dilatation of the heart which are known to clinical medicine. The enlargement is ordinarily ascribed to the accumulation of fluid in the pericardial sac, but I have had occasion to tap the pericardial sac as many as three times without obtaining any fluid whatsoever. Therefore, I believe that dilatation of the heart may occasionally be an important feature of acute pericarditis.

The clinical features of pericarditis were similar in all the cases. The pericarditis occurred in the course of an acute respiratory infection, having its onset after the first week, or in some cases when the original infection, which varied in severity from mild to severe, had about run its course. Evidence of active pericardial inflammation then persisted for as long as two or three weeks or, as in 1 case, for a much shorter time. A loud pericardial friction rub over the entire precordial area was usually audible during this entire period. Pericardial involvement was characterized by recurring sharp precordial pain, and in 2 cases by severe crushing anterior chest pain similar to that which occurs in acute myocardial infarction. Pleuritic pain was also usually present. The temperature chart may reveal but slight elevation, or a widely swinging temperature up to 104 or 105°F., while the pulse rate remains relatively slow and may show sinus arrhythmia. One patient had paroxysmal auricular fibrillation, and another paroxysmal auricular tachycardia. With the advent of pericarditis the white-cell count usually remains within normal limits or becomes slightly elevated. The corrected sedimentation rate is elevated. Once recovery sets in progress is rapid and without sequelae, and normal activity is soon possible. None of the patients have manifested residual cardiac defects; one of them has been followed for thirteen years, and another for nine years.

Cases 2, 4 and 5 occurred during a period when primary atypical pneumonia[41, 42] was prevalent and was recognized and differentiated from the usual bacterial types of pneumonia. The clinical and x-ray features in these cases were similar to those described as occurring in primary atypical pneumonia, and the presence of ordinary bacterial agents could not be demonstrated. Although staphylococcal empyema was present in Case 3, the pulmonary infection was unlike the cases of staphylococcal pneumonia that have been described,[43, 44] and its nature must remain in doubt. In this period (1933), 2 other cases of pericarditis that complicated pneumonia following a "grippe-like" infection were seen. The nature of the respiratory infection in Case 1 is also uncertain, except that the onset was like "grippe," which diagnosis, in fact, was originally made. The illness had none of the features suggesting that it might have been rheumatic carditis without valvular involvement.[45] Although pericarditis may occur as a postoperative complication,[46] including thyroidectomy,[47] the long lapse of time between thyroidectomy and the onset of pericarditis makes any causal relation extremely unlikely.

Summary

Five cases of acute pericarditis complicating respiratory infections are described. In 3 cases the characteristics of the respiratory infection were similar to those occurring in primary atypical pneumonia.

Acute cardiac dilatation was demonstrated by teleroentgenograms and was unaccompanied by evidence of disturbed cardiac function. Complete cardiac recovery occurred in every case.

Acute cardiac dilatation is not identical with acute heart failure or with any symptoms or signs of altered cardiac function. Within certain limits of time and degree it may be regarded as physiologic.

The mechanism of acute cardiac dilatation associated with pericarditis is discussed.

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THE INTRAPERITONEAL USE OF SULFANILAMIDE IN GASTROINTESTINAL RESECTIONS

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THE present concept of the mode of action of the sulfonamide compounds provides a rational basis for their prophylactic intraperitoneal use in gastrointestinal surgery, and gives good reason to believe that this may be one of the most fruitful and advantageous fields for the employment of these drugs. A brief summary of the steps leading to the present knowledge of the action of these drugs will make clear the basis for this opinion.

Lockwood[1] in 1938 demonstrated that peptones resulting from the proteolytic action of bacteria exercise an inhibitory effect on the action of sulfanilamide, and suggested that the latter prevents the specialized metabolic activity required of invasive organisms. He offered evidence that this effect may be achieved by the prevention of utilization of protein metabolites by the organism. Fildes,[2] in a study of the mechanism of the antibacterial action of mercury, found that it is specifically neutralized by sulfhydryl (SH) compounds and concluded that mercury combines with them, thus depriving the bacteria of SH groups. This conclusion, he believed, accords with the view that antibacterial substances may operate by interfering with essential metabolites necessary for the growth of bacteria. Stamp,[3] working on a similar hypothesis, found that extracts of streptococci contain a substance that antagonizes the action of sulfanilamide. Green[4] noted that under certain conditions *Brucella abortus* is capable of releasing some factor into the culture medium that inhibits the action of sulfanilamide. He showed that the yield of the antisulfanilamide factor is greater when the *Br. abortus* is allowed to autolyze. He also demonstrated that this factor has a powerful growth-promoting effect, not only on *Br. abortus* but on other organisms as well.

Previously, McIntosh and Whitby[5] and others had called attention to the fact that a particular concentration of sulfanilamide is not bactericidal to more than a certain number of bacteria, varying with the species. This observation was confirmed by Green, who noted, for example, that an inoculum of 2000 organisms in a 1:10,000 concentration of sulfanilamide showed, after a preliminary growth phase, progressive bacteriostasis and final sterilization, whereas an inoculum of 3000 organisms finally grew out. This relation was precise and constant and could be accurately predicted. Green's observations all pointed to the conclusion that the antisulfanilamide factor responsible for overcoming the bacteriostatic effect is produced by the autolysis of dead and living cells. Finally, he pointed out a fact frequently overlooked—namely, that whereas it is generally considered that sulfanilamide is bacteriostatic to relatively few organisms, it tends to be forgotten that the sensitivity to it varies only in degree, though often very widely. Not one of many organisms tested by him was completely insensitive to 1:100 concentrations of sulfanilamide. He found, for example, that a small inoculum of the almost insensitive *Bacillus subtilis* was killed by a high concentration.

Finally, Woods[6] found that yeast extracts contain a substance that, like those of Stamp and Green, reverses the inhibitory effect of sulfanilamide. The behavior and chemical properties of this substance suggested to him that it might be chemically related to sulfanilamide. Following this lead, he tested various substances having a chemical structure similar to that of sulfanilamide. One of these, *p*-aminobenzoic acid, was discovered to have a high antisulfanilamide activity. Woods found a constant relation between the concentration of sulfanilamide used and the concentration of *p*-aminobenzoic acid required to reverse its inhibitory effect. He believed that his findings provided strong confirmation of Lockwood's suggestion that the inhibitory effect of sulfanilamide on bacterial growth is based on an inactivation of bacterial enzymes, and that the inactivation is due to the competition for the enzyme between the metabolite essential for bacterial growth and the structurally similar sulfanilamide. Woods further suggested that the differences in sensitivity of different organisms to sulfanilamide inhibition are correlated with quantitative differences in ability to synthesize *p*-aminobenzoic acid.

The significance of the foregoing with respect to the prophylactic intraperitoneal application of sulfanilamide in gastrointestinal surgery will be clear when the following points are considered. Immediately after the construction of an anastomosis, whether done by an open or by a so-called "aseptic" technic, conditions exist that are most favorable for the effective action of sulfanilamide.

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The inoculum of bacteria along the suture line is small. If infection can be considered to exist at this time, it is presumably in a preinvasive stage and there is little or no protein digestion, and it may reasonably be assumed that antisulfonamide substances are not present in high concentration. By the local application of sulfanilamide along the suture line, an overwhelming concentration of the drug can be brought to bear on the small number of bacteria.

It has long been known that in the healing of anastomosed hollow viscera the first essential is the agglutination of the opposed serosal surfaces by a fibrin seal. In the absence of any gross technical error, secondary leakage of a suture line may occur as a result of bacterial action along it, causing interference with agglutination of the opposed serosal surfaces or lysis of the fibrin seal that has begun to form. If local bacteriostasis along the suture line can be maintained long enough to permit the formation of a firm fibrin seal, which requires only a few hours to take place, the danger of secondary leakage and peritonitis can be greatly diminished.

That the local implantation of sulfanilamide is effective in bringing about this result has been dramatically shown by Varco, Hay and Stevens.[7] By this method they were able to reduce to zero the mortality from peritonitis in a series of complicated experimental gastrointestinal surgical procedures on 37 dogs — procedures that had hitherto carried a discouragingly high mortality from leakage at the suture line and subsequent peritonitis. They observed further that in the few dogs in the series that died of other causes, there was found at post mortem a firm fibrin seal between the opposed serosal surfaces, which contrasted sharply with the picture observed when dogs that had not been treated with sulfanilamide died of peritonitis in this interval, where there was little fibrin sealing and, hence, gross contamination from the stitch holes.

We have to date used sulfanilamide as a prophylactic agent by local implantation within the peritoneal cavity in 75 cases of gastrointestinal anastomosis or other operative procedures requiring the opening and closure of hollow viscera within the peritoneal cavity, excluding obstructive or Mikulicz resections. These cases are summarized in Table 1.

Sulfanilamide was used as the chemotherapeutic agent in all cases. The chemotherapy was limited to the intraperitoneal dose, with the single exception of a case of carcinoma of the sigmoid in which sulfaguanidine was given orally both preoperatively and postoperatively. We believe that this point is of major significance with respect to the incidence of toxic reactions. This has been emphasized by Jackson and Coller,[8] who observed no toxic reaction in a series of 33 cases in which sulfanilamide was given only intraperitoneally. In contrast with this, they report 9 cases of toxic hepatitis with jaundice in a series of 29 cases in which additional sulfanilamide was given. In our series, there was but one clear-cut toxic reaction, a toxic hepatitis occurring four days after a gastric resection. Complete recovery followed a stormy convalescence.

TABLE 1. *Data on Cases.*

OPERATIVE PROCEDURE	No. OF CASES	No. OF DEATHS
Gastric resections (1 transthoracic)	39	5
Taking down posterior gastroenterostomy; excision of gastrojejunocolic fistula and gastric resection	3	
Taking down posterior gastroenterostomy; excision of gastrojejunal ulcer	1	
Posterior gastroenterostomy	5	
Gastroduodenostomy	1	
First-stage Whipple type of operation; posterior gastroenterostomy; cholecystjejunostomy and jejunojejunostomy	1	
One-stage duodenectomy; posterior gastroenterostomy; cholecystjejunostomy	1	
Right colectomy	6	1
Ileotransverse colostomy	4	
Resection of colon and rectosigmoid	7	
Sigmoidotomy and polypectomy	1	
Reduction of partial intussusception and excision of lipoma of colon	1	
Resection of ileum	3	
Taking down of end ileostomy; ileocecostomy	1	
Excision of cutaneocolic fistula	1	
Totals	75	6

In the case in which sulfaguanidine was given preoperatively and postoperatively, mentioned above, a toxic hemolytic anemia was suspected on the second postoperative day, when the red-cell count and hemoglobin suddenly dropped from preoperative levels of 4,510,000 and 90 per cent, respectively, to 2,600,000 and 54 per cent. However, on the same day there was a discharge of dark blood from the wound, and subsequently large quantities of dark blood were passed rectally. We are inclined to believe that this represented a straightforward case of postoperative hemorrhage, rather than a reaction to the drug.

We are convinced that the danger of serious toxic reaction is slight when a single intraperitoneal dose of sulfanilamide is used, even when this dose is large.

The intraperitoneal doses of sulfanilamide employed in our series varied from 4 to 16 gm., with an average of 7.8 gm., and in 10 cases an additional amount (2 to 4 gm.) was left in the wound. When this study was first begun, we were influenced in favor of relatively large doses by the experience and recommendations of Thompson, Brabson and Walker[9] in the intraperitoneal use of sulfanilamide in appendicitis. In the more recent cases, the usual intraperitoneal dose has been 6 to 8 gm.

Whereas sulfanilamide alone was used in all our cases, it seems likely that a mixture of sulfanilamide and sulfathiazole, as advocated by Key[10] in orthopedic conditions, offers certain advantages. Throckmorton[11, 12] has shown that in experimental animals some sulfathiazole remains visible within the peritoneal cavity for three to six days after implantation, whereas sulfanilamide remains visible for only six to twelve hours. The prolongation of the local effect that would be attained by the use of the more slowly absorbed sulfathiazole, its wider range of bacteriostatic activity and its more effective mobilization of cellular reaction all lead us to believe that a mixture of sulfathiazole and sulfanilamide may offer definite advantages.

In the series of 75 cases, there were 6 deaths, a mortality of 8 per cent. There were no deaths from peritonitis. Pulmonary embolism was the cause of death in 3 cases. In 2 of these, both gastric resections, the diagnosis was confirmed by autopsy. In the third case, a right colectomy, autopsy was not done, but the embolism occurred on the eighteenth postoperative day, when the patient was ready to be discharged.

In 2 of the remaining fatal cases, both gastric resections, the cause of death was pneumonia. In 1 of these cases, two of the silkworm-gut stay sutures gave way on the fifth postoperative day and dehiscence of the wound requiring resuture occurred, following which the patient developed pneumonia. Although death was clearly due to pneumonia, at autopsy an unsuspected pelvic abscess and an abscess in the right lumbar gutter were found, although all visceral suture lines were intact and there was no evidence of leakage. This patient had had a large polypoid carcinoma of the stomach that contained an intramural abscess with acute inflammatory changes in the adjacent tissues, which may, perhaps, have led to peritoneal contamination by organisms of unusually high virulence. Autopsy was not done on the second case, but clinically, death was due to pneumonia. The sixth fatality was in a transthoracic gastric resection, fifteen weeks after operation. An esophagogastric fistula with empyema and inanition was the cause of death.

Additional wound complications comprised minor infection in 3 cases, major wound infections in 2, transient pancreatic drainage after duodenectomy in 1, and transient duodenal fistula in 1. The last occurred in a case in which the duodenum was divided a few millimeters above the papilla of Vater. There was one other wound dehiscence, after a right colectomy, apparently due to mechanical factors. An incarcerated loop of small intestine distant from the anastomosis perforated and resulted in a local peritonitis. This occurred, however, after the anastomosis had begun to function. This patient still has an ileal fistula but is recovering.

Summary and Conclusions

A series of 75 cases of gastrointestinal anastomosis, or some other operative procedure in which opening and primary closure of one or more hollow abdominal viscera were done, is reported in which sulfanilamide was applied intraperitoneally along the suture lines in the viscera. There were no deaths from peritonitis. Clear evidence of intraperitoneal infection was observed post mortem in only 1 fatal case, and in this case was not the cause of death. Only 1 patient had a toxic reaction to the drug, a toxic hepatitis with recovery.

Our experience with this series has convinced us of the value of the local intraperitoneal use of sulfanilamide along the suture lines after gastrointestinal anastomosis and in all cases with peritoneal soiling. We are satisfied that the danger of serious toxic reaction to the drug is slight if the intraperitoneal dosage does not exceed an average dose of 8 gm. in adults, and if this dose is not immediately preceded or followed by the additional administration of a sulfonamide.

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THE ANTI-THIAMINE FACTOR IN FISH*

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EPIDEMICS of a severe and unusually fatal paralytic disturbance have been observed in animals when fish has been added to their diet.[1-10] A review of the circumstances of these epidemics of so-called "fish disease" and a study of the factor in fish responsible for them permit certain conclusions to be drawn concerning the use of fish in diets intended for human consumption.

FISH DISEASE IN ANIMALS

In 1936 Green[1] described a syndrome in foxes that was induced by adding fresh fish to their diet. The clinical and pathological features of the disturbance resemble those of Wernicke's syndrome in man.[11-13] The first symptom is anorexia, which is usually followed in a few days by weakness, hyperesthesia, ataxia and death.[1-10] Postmortem examination of the central nervous system reveals proliferation of the endothelium and adventitia of the small blood vessels, with varicose deformities and bilaterally symmetrical hemorrhages in the paraventricular nuclei and in the gray matter of the brain stem.[11-13] Studies of the cord and peripheral nerves are not reported, but degenerative lesions of the myocardium and fatty infiltrations of the liver have been described. Pups nursing from mothers affected with the disorder die early, without the histologic changes seen in the older animals.[14]

The disease is evidently one of thiamine deficiency, since it may be produced by thiamine deficiency under experimental conditions[15,16] and may be cured by thiamine injections.[4-6, 8] The exact distribution of the factor in fish responsible for production of the deficiency has not been surveyed. The disease, however, has been observed following the consumption of carp, Atlantic Coast whiting, Pacific Coast mackerel, Lake Superior and Lake Michigan herring, suckers, smelts, mullets and great northern pike.[7,9] Experiments with carp have demonstrated that the factor responsible is present in large quantity in the viscera and to a less extent in the heads, skin and scales. It does not seem to be present to a significant extent in the fish muscle. Thus, diets containing 20 per cent of fish muscle were found to be innocuous, whereas diets containing 10 per cent of whole raw fish promptly produced symptoms.[6,8]

Of critical importance, however, is not the amount of fish present in the diet, but rather the thiamine content of the diet as a whole and the length of time during which fresh raw fish is allowed to stand in contact with the thiamine-containing foods.[15, 16] Intimate mixing of the thiamine-containing constituents of the diet with portions of raw fish rich in the anti-thiamine factor is essential to production of the disease. Raw fish fed as a separate meal is harmless.[6]

CHARACTERISTICS OF THE ANTI-THIAMINE FACTOR

The anti-thiamine factor is destroyed by cooking,[15] and also by drying in air at room temperature.[16] The factor is of large molecular size and does not pass the membrane of living cells.[16, 17] It may be precipitated by protein precipitants and destroyed by peptic digestion.[18, 19] The reaction with thiamine appears to be enzymatic and to exhibit maxima at pH 9 and 60°C.[18] Tables 1 and 2 illustrate the effect of pH and temperature on the rate at which the anti-thiamine factor of carp destroys thiamine.

TABLE 1. *Effect of pH on the Destruction of Thiamine by Carp Enzyme.*§

pH	Thiamine Destroyed
	%
6	40
7	60
8	90

§1 cc. of carp extract, 4 cc. of phosphate buffer and 25 microgm. of thiamine, incubated for 30 minutes at room temperature.

TABLE 2. *Effect of Temperature on the Destruction of Thiamine by Carp Enzyme.*‖

Temperature (Centigrade)	Thiamine Destroyed
	%
6°	30
29°	60
46°	100

‖1 cc. of carp extract, 4 cc. of phosphate buffer (pH 7.0) and 25 microgm. of thiamine, incubated for 30 minutes.

CONCLUSIONS

From the foregoing review it appears that there is present in the viscera, heads, skins and scales

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of certain fish a proteinlike material capable of destroying thiamine in a manner suggestive of an enzymatic reaction. When portions of fish containing this anti-thiamine factor in significant quantity are allowed to come into intimate contact with the thiamine-containing constituents of the diet, the thiamine content of these foods may be lowered to a level no longer compatible with the maintenance of normal nutrition. Epidemics of thiamine deficiency explainable on this basis have been observed in animals to whose diet fresh raw fish has been added. Similar epidemics have not been observed in man.

There are a number of reasons why thiamine deficiency of this particular mechanism of origin may not be frequent in man. The portions of fish that are rich in anti-thiamine factor are for the most part those usually discarded in the preparation of fish for human consumption, that is, viscera, heads, skins and scales. Moreover, the destructive reaction with thiamine is definitely extrinsic since the factor itself is destroyed by peptic digestion. Because the factor is also destroyed by cooking or by drying, the only opportunity for its significantly affecting thiamine nutrition lies in those occasions where the major thiamine-containing constituents of the diet are mixed with whole raw fish and the mixture is allowed to stand at room temperature for some time before being cooked, eaten or dried. Under ordinary circumstances of diet preparation such circumstances are rare.

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MEDICAL PROGRESS

GENERAL ANESTHESIA

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THE present-day utilization of new anesthetic agents, modern gas machines, improved technics and certain combinations of agents has given general anesthesia a flexibility and safety indicative of important progress in recent years.

The gas machine, the principal item in the anesthetist's armamentarium, not only enables him to administer anesthetic agents economically and conveniently but also aids in the maintenance of normal physiology, reduces the explosion hazard and provides an immediately available means of resuscitation. A modern gas machine used in conjunction with an endotracheal tube is practically indispensable for the application of positive intrapulmonary pressure in intrapleural surgery.

The following is a summary of the present status of the various agents used for general anesthesia.

INHALATION ANESTHESIA

Established Agents

Diethyl ether remains the standard drug for inhalation anesthesia, because of its wide margin of safety, relatively low toxicity, economy, and ease of administration, especially by the open-drop method. Since the characteristic effects of ether are well known, their discussion in this article is unnecessary.

If considerable quantities of ether are used, a marked saving in cost may be achieved by bulk purchases. The *United States Pharmacopoeia* no longer states that ether is unsatisfactory for use twenty-four hours after the container is opened, and approves the use of 3-liter containers for storage. Ether is entirely satisfactory for clinical use for long periods after the seal of the container is broken,[1] and the use of 5-pound to 50-pound drums has been recommended. With proper precautions, ether may be drawn with perfect safety from the large containers into suitable small ones for operating-room use.

Cyclopropane is thought to be the most nearly ideal anesthetic agent, because of its potency, rapidity of induction and recovery, apparent lack of toxicity, pleasantness to the patient and the high percentage of oxygen employed in administration. Whether it merits such a position is still debatable. When mixed with oxygen, it is highly explosive, and should be used only by one familiar with its toxic characteristics, since its action is rapid and the signs of degree of anesthetic depth are not so clear cut as those when ether is used.

The most commonly noted undesirable effects of cyclopropane are the various cardiac arrhythmias. They occur most frequently under deep anesthesia but also are observed under light anesthesia. Their control remains a problem, and whether they leave any long-lasting damage has not been determined. Arrhythmias may sometimes be inhibited by the simultaneous use of procaine.[2] The protective action of the barbiturates has been confirmed[3] and also denied.[4] Morphine tends to exaggerate arrhythmias,[2,3] and if large doses are used preoperatively, marked depression of respiration is likely to occur. The concomitant administration of cyclopropane and epinephrine is prone to produce ventricular fibrillation.

Since cyclopropane may have a tendency to act as a cardiac irritant, it probably should not be used in patients with cardiac impairment or with thyrotoxicosis. There have been reports of sudden deaths on the operating table of patients with thyrotoxicosis receiving this agent as an anesthetic. These deaths were probably due to ventricular fibrillation.[5]

Even in deep anesthesia troublesome laryngospasm occurs at times when high concentrations of cyclopropane are employed or when traction is exerted on the abdominal or pelvic organs.[6]

In most patients in whom a general anesthetic agent is indicated, with the exception of those undergoing abdominal surgery, cyclopropane produces satisfactory anesthesia. The degree of relaxation obtainable with safety is less than that obtained with ether; however, Guedel[7] has offered a controlled-breathing technic to eliminate this difficulty.

As a supplemental agent for regional or spinal anesthesia, cyclopropane has proved valuable.[8] In the presence of nausea, psychic disturbances or inadequacy of the principal agent, its use frequent-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas. 1942. $5.00).

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ly makes an otherwise unsatisfactory situation tolerable to both the surgeon and the patient. Cyclopropane has been used in obstetrics with good results.[2]

Ethylene is probably the most nontoxic of all inhalation agents with appreciable potency. Although explosive in anesthetic mixtures with oxygen, when properly used in patients with cardiac abnormalities it is safe and well tolerated. In many types of cases ethylene might well be employed with greater frequency. The concentrations required are comparable to those of nitrous oxide, but it is more potent than the latter, produces better relaxation and permits the use of somewhat higher percentages of oxygen.

Nitrous oxide is a relatively weak anesthetic gas. With an adequate percentage of oxygen, it is safe, but such a mixture frequently gives inadequate anesthesia, and consequently the flow of oxygen is reduced to a dangerous level. Sufficient morphine or a barbiturate given preoperatively often allows adequate anesthesia to be obtained with safe concentrations of nitrous oxide. Following the rectal administration of tribromethanol (Avertin) or Pentothal sodium, nitrous oxide is a most satisfactory anesthetic agent for many types of extra-abdominal operations. This combination is pleasing, especially to apprehensive patients or children, and is well tolerated by many poor-risk patients.

Ethyl chloride is a toxic drug with a narrow margin of safety.[9] For general anesthesia it is dangerous because of its inherent tissue toxicity and because of its volatility, which may result in its vapor's rapidly displacing air in the air passages, with absorption of an overdose before the flow is controlled. A slow dropping on a gauze mask — not a spray — is the administration method of choice. Ethyl chloride should not be administered by one inexperienced in its use, but in the hands of a skilled anesthetist it is satisfactory for brief surgical procedures and as an induction agent preceding ether.

Chloroform is still considered too dangerous for frequent use. In addition to its toxicity to the liver and heart, it diminishes the plasma prothrombin,[10] with consequent probable increase in bleeding hazards.

Divinyl ether (Vinethene) should not be considered a substitute for ether or cyclopropane. Because of its toxicity, it is contraindicated when hepatic or renal damage exists.[11] Because induction and recovery are rapid and because the drug is potent and causes little respiratory irritation, it has proved satisfactory for short surgical procedures requiring light anesthesia. Divinyl ether is administered preferably by the open-drop method and is suitable for children, especially as an induction agent for diethyl ether. If divinyl ether is to be used for longer than thirty minutes, it should be volatilized with oxygen. This probably affords some protection against liver damage.[12]

New Agents

With the idea that new substances structurally resembling cyclopropane, ethylene and diethyl ether might be synthesized and proved to be valuable anesthetic drugs, a considerable number of chemicals have been developed. Some of them possess anesthetic qualities but because of toxicity or undesirable side effects are impractical for clinical use. However, *cyprome* and *cyclopropylmethyl ether* have been used with good results. *Cyprethylene ether*, first used in human subjects in November, 1941, is even more promising.[13] It presents a high potency, produces marked relaxation, and can be administered in a mixture with high oxygen concentration.

For many years *trichlorethylene* has been known to possess anesthetic qualities. During the last eight or ten years a study of its characteristics and its effects on human beings has shown certain desirable qualities.[14] Trichlorethylene has only a minor degree of toxicity for the liver and kidneys, produces little irritation of the respiratory passages, has slight effect on the body chemistry and decreases capillary oozing. In spite of these admirable qualities, trichlorethylene is used but little because vaporization is difficult, which makes it unreliable for third-stage anesthesia, and because in many cases inadequate muscular relaxation results.

Although trichlorethylene is usually considered to be noninflammable,[15] recent work has shown that, whereas this is true for mixtures of air and trichlorethylene under ordinary conditions of temperature and pressure, it is probably not true of mixtures of this drug with pure oxygen. Recently published figures indicate that mixtures of trichlorethylene and oxygen are inflammable within the limits of 10.3 per cent to 64.5 per cent trichlorethylene.[16]

It has recently been shown that this drug is capable of producing cardiac arrhythmias,[17] an undesirable feature in anesthesia.

Tetrachlorethylene, a nonexplosive, noninflammable liquid with anesthetic properties, is probably nontoxic.[18] In man a moderate degree of surgical anesthesia can be produced, but its disadvantages probably make it of little value clinically. Tetrachlorethylene is difficult to volatilize and is irritating to the mucous membranes and the skin.[18]

Explosion Hazards

Although anesthetic mixtures in oxygen of ether, cyclopropane and ethylene are explosive, they are safe when proper precautions are taken to prevent static sparks and to exclude cautery or sparking electric apparatus from the vicinity. Modern operating rooms in which switches and wall plugs are designed to minimize the possibility of igniting inflammable mixtures, and in which good ventilation is provided, together with the use of an intercoupler and a tightly closed breathing system, have done much to eliminate the explosion hazard. The likelihood that a spark or flame will ignite a mixture decreases markedly when its distance from the leaking mixture is two feet or more.

Efforts have been made to find a suitable combination of an anesthetic agent, oxygen and an inert gas—for example, helium—that is nonexplosive. Several such combinations have been devised.[19] Their practical value is doubtful, however, because not much variation in the relative proportions of their constituents is possible. Present-day gas machines are not considered accurate enough to allow their use with any degree of safety.

Rectal Anesthesia

The most widely used drug for rectal anesthesia is *tribromoethanol* (Avertin) *in amylene hydrate*. It was originally intended for use unsupplemented, but since the doses required proved too depressing, it is now employed as a basal anesthetic. In combination with nitrous oxide, it furnishes excellent anesthesia in thyroid surgery.[20] In apprehensive patients and children, its use does much to allay preoperative fear and facilitates rapid, smooth induction of anesthesia.

This drug might be more widely used for basal anesthesia except that it often produces a prolonged period of postoperative respiratory depression, tending to allow secretions to accumulate in the respiratory passages. This lengthy period of postoperative unconsciousness necessitates more intensive nursing care.

Pentothal Sodium, although primarily intended for intravenous anesthesia, has proved an effective and safe basal anesthetic when given rectally and followed by nitrous oxide or a small amount of cyclopropane.[21] The action of the drug when administered rectally is essentially the same as that when given by the conventional intravenous route. Rectal installation should take place half to one hour previous to beginning the inhalation phase of the anesthesia. In healthy adults the dose is 1 cc. of a 10 per cent solution for every five pounds of body weight. A smaller dose is used when indicated by the patient's age or condition.[21] In infants, Pentothal Sodium has been used in this manner in doses of 0.8 cc. of a 2.5 per cent solution per pound of body weight.[22]

Evipal Soluble is also a satisfactory basal anesthetic when given rectally one hour preceding the inhalation anesthetic in doses of 0.2 cc. of a 10 per cent solution per pound of body weight.[23]

Intravenous Anesthesia

Clinically intravenous anesthesia is today achieved almost solely by the use of *Pentothal Sodium* or *Evipal Soluble*, the two outstanding short-acting barbiturates. The former drug is given the preference by most anesthetists in their routine work, since the rapidity of induction and the infrequency of postoperative nausea and vomiting make it most acceptable to patients.

When Pentothal Sodium is the sole anesthetic agent, the surgical procedure is limited generally to forty-five minutes and does not require a considerable degree of muscular relaxation. A wide variety of difficult types of surgery, including intra-abdominal procedures, have been performed successfully under Pentothal Sodium alone, but when one considers the danger to the patient of the required deep anesthesia and the technical difficulties that the surgeon is likely to encounter in its frequent use, it seems best in such cases to rely on other agents commonly available in civilian practice.

In military surgery, however, especially under front-line conditions, Pentothal Sodium is an extremely valuable and widely used drug. One surgeon[24] in describing his experience in treating battle casualties said that the wounded men were brought in frightened, heavily narcotized, tired and in more or less shock. The necessary surgical procedures usually required not over an hour, and in about 95 per cent of the cases intravenous anesthesia was employed. In the Dieppe raid, Pentothal Sodium was used as the sole anesthetic agent in treating 51 per cent of the casualties.[25] The usual rapid recovery from the anesthetic agent with few aftereffects allowed rapid evacuation of the patients to hospitals some distance from the front. Since Pentothal Sodium is noninflammable and easily transported, prepared and administered, it is highly acceptable under these conditions.

The scope of intravenous anesthesia has been greatly widened by its use in combination with other methods. As a supplement to spinal anesthesia, it eliminates the nausea, retching and painful traction stimuli often accompanying abdominal procedures, and does not cause the increased diaphragmatic excursions often noted when an inhalation anesthetic agent is used as a supplement.[8] Electric apparatus and cautery may be employed freely when a spinal anesthetic and Pentothal Sodium are used.

Combined with local infiltration, regional or splanchnic block or nitrous oxide, Pentothal Sodium produces good anesthesia, especially for poor-risk patients.[26] Diabetic patients also tolerate the drug very well.[26] Certain hazards accompany its use, and the anesthetist should be prepared with means for combating them. Respiratory failure may result from an overdose or from laryngospasm. The latter is especially prone to occur in the presence of excessive amounts of mucus or blood or when instrumentation in the pharynx is performed. Laryngospasm may be prevented if the pharynx and glottis are sprayed with a 10 per cent solution of cocaine immediately prior to the injection of the Pentothal Sodium. Hiccups occurring under the drug usually cease if intravenous atropine (1/75 gr. in adults) or cyclopropane is administered. Atropine should be given routinely before intravenous Pentothal Sodium, and a preoperative sedative such as morphine allows the use of smaller doses.[27] The continuous administration of 100 per cent oxygen during the anesthesia has been recommended. On the basis of animal experiments, Beecher and Moyer[28] have questioned the wisdom of giving 100 per cent oxygen to patients with respiratory depression under Pentothal Sodium anesthesia; ordinarily a low concentration of oxygen in the blood stimulates the respiratory center when the sensitivity to carbon dioxide is diminished, and the use of 100 per cent oxygen removes this stimulus. The use of Pentothal Sodium anesthesia is also considered unwise when hepatic, renal or serious cardiac disease exists, or when any condition that may interfere with adequate pulmonary ventilation is present.[27]

Although the subject is controversial, some reports indicate that the barbiturates tend to prevent or retard the onset of shock.[26, 29]

Clinically, there is ample evidence that Pentothal Sodium is not contraindicated when the patient has been receiving sulfonamide therapy.[27]

Pentothal Sodium may also be used as an induction agent prior to the administration of the principal agent and, if desired, can be given in the patient's room. This drug is valuable as an anticonvulsant.

Pentothal Sodium may be prepared in bulk solution. Five grams of the drug in 200 cc. of sterile distilled water gives a 2.5 per cent solution, which is satisfactory for use for several days or as long as the solution remains clear. This concentration is the one most widely used at present, since better control of the dosage is obtained, since accidental extravenous injection is less likely to produce undesirable tissue damage and since the incidence of phlebitis is decreased.

Recently published data show that the use of *paraldehyde* as an intravenous anesthetic agent has probably been responsible for a number of deaths.[30] Animal experiments confirmed the fact that paraldehyde was no doubt the cause of the post-mortem findings in these cases. With this in mind, paraldehyde should not be used for intravenous anesthesia, especially since Pentothal Sodium is safe and is readily available in most hospitals.

Premedication

Morphine, the *barbiturates* and the *belladonna derivatives*, atropine and scopolamine, continue to maintain their status as the standard drugs for preoperative medication. Morphine may be administered intravenously a few minutes before the induction of anesthesia, if the usual subcutaneous dose was omitted or proved insufficient to produce the desired sedation in a reasonable length of time.[31] Morphine by the intravenous route should be given slowly, preferably in smaller doses than when given subcutaneously, and administration should be stopped if dizziness, numbness, tingling or other untoward reactions occur.[31]

A new synthetic drug, *1-methyl 4-phenyl-piperidine 4-carboxylic acid ethyl ester hydrochloride* (Demerol), has made its appearance as a substitute for morphine, especially if the supply of the latter should be threatened because of wartime conditions. It is one of a series of piperidine compounds, resembles atropine structurally, and possesses some of the properties of the latter, in addition to being a satisfactory analgesic and sedative. Demerol is said to be comparable to morphine and to be as reliable as the latter in the recommended dosage. The atropine-like properties of the drug are its ability to cause drying of the mucous membranes and its spasmolytic effect. Since it does not depress the cough reflex as does morphine and is effective for pain originating in serous membranes and smooth muscle, it may prove to be valuable in postoperative treatment. Whether its continued use will result in habituation has not been determined.[32,33]

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**
BENJAMIN CASTLEMAN, M.D., *Acting Editor*
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CASE 29361

PRESENTATION OF CASE

First admission. A thirty-five-year-old volunteer war worker entered the hospital because of paresthesias of the fingers of nine weeks' duration.

For the previous nine weeks he had noticed tingling of the fingers; he had become noticeably weak, especially in the arms. His physician found the hemoglobin to be 65 per cent and gave him iron and cod-liver oil without any benefit. During the week before entry the tongue felt thick.

At the age of twenty-two he began to lose weight; he was told that his systolic blood pressure was 200 and that "he was threatened with tuberculosis." He went south, "took it easy" for four years and had worked hard ever since. The hypertension apparently disappeared. About a year before entry he was turned down by the draft-board physician for a cardiovascular defect, but was not told what it was.

Physical examination on admission showed a well-developed, well-nourished man. There was slight diminution to light touch and pinprick around the mouth. The tongue was slightly tremulous but not atrophic. The upper extremities were normal in color and ability to sweat. The strength of all muscle groups was definitely weakened, most conspicuously in the shoulder girdles—he could barely raise his arms above his head. There was no muscular fibrillation. He could not stand or walk on his toes or heels, or rise from a squatting position. The abdominal and back muscles were relatively strong. The Romberg sign was positive. There was no muscle tenderness, but straight leg-raising carried to 45° caused pain bilaterally. There was sensory loss for touch and pain in the distal portions of the arms and legs. Vibratory sense was diminished over the wrist, and lost over the malleoli. The triceps reflexes were barely present; the biceps, radial, ankle and knee jerks were absent; abdominal and cremasteric reflexes were present. The heart, lungs and abdomen were normal.

The blood pressure was 134 systolic, 106 diastolic. The temperature and respirations were normal; the pulse was 84.

The white-cell count was 8700, with 66 per cent neutrophils, and the hemoglobin 14.5 gm. The urine was normal. A gastric analysis was normal. A blood Hinton test was negative. A lumbar puncture gave an initial pressure of 150 mm. (water). There were no cells in the spinal fluid; the total protein was 133 mg. per 100 cc., and the gold-sol curve 0011222200. A spinal-fluid Wassermann test was negative.

X-ray examination of the chest revealed no definite increase in the size of the heart. The apex of the heart was somewhat rounded, and the aorta was slightly tortuous; the lungs and the diaphragm were normal.

The patient was discharged, unimproved, after five days.

Final admission (two weeks later). The patient returned because of difficulty in breathing. After his discharge there was gradual progression of weakness. On one occasion he fell and had difficulty getting back to bed. For two days prior to admission there was some difficulty in breathing, and slight difficulty in swallowing and talking. There was no increase in sensory symptoms.

The weakness had increased, and it involved not only the arms and legs but also the abdomen, back and neck and intercostal muscles. Chest expansion was limited to 3 cm. at the level of the nipples. The voice was husky and frequently trailed off into a whisper. The facial, ocular and masseter muscles seemed to be normal. All the tendon reflexes, as well as the abdominal and plantar reflexes, were absent.

The blood pressure was 140 sytolic, 100 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

The patient was given hot packs (Kenny therapy). He developed cramps of the flexors of fingers of both hands, which recurred during his entire stay. On the third day he had so much respiratory difficulty that he had to be put into a respirator. Following this episode he was able to elevate his arms overhead and to raise his legs from the bed, but his fingers and toes remained very weak. There was preservation of the sensations of light touch and pinprick throughout. Profound disturbance of the vibration and position senses was noted in all extremities. There was minimal tenderness of the calf muscle. A lumbar puncture gave an initial pressure of 100 mm. (water), and the spinal fluid contained no cells; the total protein was 190 mg. per 100 cc.

During the next two weeks, treatment with hot packs was carried out. On the whole there was

*On leave of absence.

no improvement or any definite progression. One observer stated that there was slight bilateral facial weakness. Toward the end of this period, however, the respirations became increasingly shallow, rapid and labored. Examination at that time revealed more tenderness and perhaps more weakness. Sinus arrhythmia, with a rate of 104, developed. The blood pressure was 150 systolic, 115 diastolic. Examination of the lungs was unsatisfactory, but they seemed to be clear.

On the twentieth hospital day the patient became weaker and was unable to raise secretions or to swallow, or to breathe outside the respirator. He died on the twenty-first hospital day.

Differential Diagnosis

Dr. Augustus Rose: I assume that discharge from the hospital at the time of the first admission was not because the attending physician believed that the patient was over his illness. There undoubtedly were other reasons, economic or something of that nature. There is no mention of mental symptoms, so I shall assume that the patient was normal mentally.

This case offers little or no difficulty in diagnosis, yet it raises the important question of polyneuritis and a discussion of the pathology of the condition. Ignoring the details of the history, this is the case of a thirty-five-year-old man who, after nine week of paresthesia and weakness of the extremities, developed cranial-nerve palsies and died in respiratory paralysis. The spinal fluid showed a high total protein without cells. This is the clinical picture, but fortunately is not the usual outcome of the condition known as infectious polyneuritis. It also goes under a number of other names: infective neuronitis, radiculoneuritis, polyneuritis with facial diplegia, Guillain–Barré syndrome and so forth.

Polyneuritis is a clinical picture, the essential feature of which is impairment of function of many peripheral nerves, resulting in a more or less symmetrical distribution of muscular weakness and sensory loss. This general picture is usually present in all cases regardless of the etiology of the neuritis. In many cases, however, there are characteristic clinical differences between the various types of polyneuritis. In most types of peripheral neuritis the weakness and sensory loss are chiefly confined to the distal portions of the extremities. In infectious polyneuritis, as illustrated by this case, muscular weakness also involves the proximal muscles of the extremities and the muscles of the trunk. In addition, muscles innervated by the cranial nerves arising from the pons and medulla are often partially or completely paralyzed.

The etiology of polyneuritis remains somewhat confused. In recent years we have heard more and more about vitamin deficiency, with evidence accumulating to show that a number of different factors contribute to the clinical picture. The role of vitamin deficiency is seen to contribute to the neuritis associated with diabetes, pregnancy and certain other metabolic and toxic conditions. It has been stated to be due to a virus, transferable to monkeys, but this has not been verified. Clinical evidence, however, supports the idea of an infectious agent. Characteristically the syndrome so well described in this case comes on a few days following a mild systemic infection in which there is a mild elevation in temperature, coryza and general malaise. Frequently also, the onset of neuritic symptoms is accompanied by slight fever. The absence of these symptoms in this case, however, does not alter the probable diagnosis, for the systemic infection may be so mild that it is overlooked or forgotten by the time the more dramatic paralytic symptoms develop. The spread of symptoms is usually fairly rapid and, not infrequently, may ascend from the lower extremities, reaching the neck and bulbar-supplied muscles last. This type of spread has led some observers to infer that the disease is located in the spinal cord as well as in the peripheral nerves. In such cases the old question of Landry's ascending paralysis is considered in the differential diagnosis, although that is only a name applied to a train of symptoms and is not a disease entity. In 1927, Dr. Viets[1] published a series of cases from this hospital in which he stressed the frequency of bilateral facial weakness without evidence of involvement of other cranial nerves. In the cases of this group coming to autopsy, pathologic changes were found in the motor cells of the spinal cord and brain stem.

Great emphasis should be placed on the spinal-fluid findings in infectious polyneuritis. The high total protein, which is almost always present in varying degree, is not accompanied by an increase in the cells. This dissociation was emphasized by Guillain, Barré and Strohl[2] and has come to be almost pathognomonic.

Returning to this particular case, I see no reason for believing that the low hemoglobin or the signs of cardiovascular disease played any role in the patient's final illness. He certainly had a mild degree of hypertension — as shown by a persistently elevated diastolic pressure and by rounding of the cardiac apex by x-ray. There are no leads suggesting disease other than that within the nervous system, or any specific etiologic agent, such as arsenic or alcohol.

It is not safe for one to put all his eggs in one basket. Yet I am at a loss to suggest any diagnosis other than infectious polyneuritis. I shall be interested in hearing a discussion of the pathology of the case by Dr. Kubik. He has often told us

that the pathology is confined to the peripheral nerves and characterized by round-cell infiltration.

Dr. James B. Ayer: This patient was under my observation for the greater part of his illness. The diagnosis was made on the first admission, at which time he was discharged slightly improved, apparently just from rest in bed. Later he developed respiratory difficulty and was sent back to be near a respirator.

I question whether there was a sensory disturbance of the face. Sensory disturbance in the cranial nerves in this disease are extremely rare. I was never convinced that he had facial paralysis, and only once did anyone think he had it; I repeatedly looked for it because it is so characteristic.

There was no evidence of cerebral involvement. The patient was always intelligent, and there was nothing that suggested encephalitis. Regarding the Kenny treatment, both legs and arms were more comfortable when packed; even respiration was benefited, and one could get about 1 cm. greater respiratory excursion after the Kenny pack had been applied to his chest. He thought it was better than the respirator, which was surprising to me, and I suggest this as an agent to be used in such cases.

We could never make any diagnosis other than what Dr. Rose has made.

Dr. Henry R. Viets: I saw this man during the last week of his illness. On at least one occasion I thought he had lower facial paralysis, but it was partial and certainly not marked.

It seems to me there is no question about the diagnosis. The most difficult point in regard to polyneuritis from the clinical point of view is the prognosis. This man was a young, husky individual, and all during the course of his illness both Dr. Ayer and I were doubtful about the prognosis, even believing at times that he might recover. Certainly we have had patients as sick as he was up to the last day of his illness who have made a total recovery. One of the surprising things is that they do recover so well and recover so completely in view of the seriousness of their illness. The fact that, in this case, the shoulders were severely involved almost from the start made me a little cautious about the prognosis because the lesion was getting close to the fourth cervical segment, where the phrenic nerve comes off. We should have taken more into consideration that he was close to the danger line at all times.

Clinical Diagnosis

Infectious polyneuritis.

Dr. Rose's Diagnosis

Infectious polyneuritis.

Anatomical Diagnosis

Infectious polyneuritis.

Pathological Discussion

Dr. Charles S. Kubik: There have been 5 or 6 deaths from infectious polyneuritis in this hospital, with autopsies in 3 of them. In the other 2 autopsied cases, death occurred on about the tenth day of the illness. This one was unusual. The steady progression of symptoms continued for approximately fifteen weeks and eventually resulted in death. The pathological findings have been essentially the same in all three cases.

The outstanding feature is an infiltration of spinal nerve roots, spinal ganglions and peripheral nerves with lymphocytes (Fig. 1). Special stains show degenerative changes in the myelin sheaths

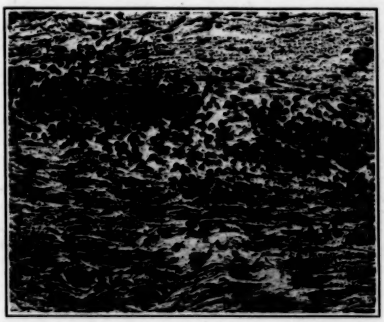

Figure 1. *Lymphocytic Infiltration of Peripheral Nerve.*

and axis cylinders, but only rarely complete destruction of fibers. Except for an axonal reaction in the anterior-horn cells, secondary to the degenerative changes in the nerve roots and nerves, nothing abnormal is found in the spinal cord, brain stem or brain.

Dr. Rose: So the disease is not entirely peripheral in an anatomic sense.

Dr. Kubik: I should consider the nerve roots as part of the peripheral system. In any case, there is no cellular infiltration in the brain or cord.

We have found pathologic changes in all cases, although it is sometimes said that there are no distinctive lesions. Since they were found in only a few out of many sections of peripheral nerve in this case, it is easy to understand why these lesions

may be missed. I should suspect that the negative findings are based on cases of deficiency neuritis that were mistaken for cases of infectious polyneuritis. Although the two conditions may resemble each other clinically, they probably have nothing in common so far as etiology is concerned. I might add that there is no cellular infiltration of the nerves in deficiency neuritis. As Dr. Rose has said, there is no good proof that infectious polyneuritis is really an infection. Bradford, Bashford and Wilson[3] thought that they had transmitted the disease to monkeys, but their claims have not been confirmed. Material from 2 of our cases was inoculated into the brains of monkeys with negative results.

DR. ROSE: Has there been, to your knowledge, any case in this hospital in which there were cerebral symptoms?

DR. KUBIK: I do not know of any.

DR. ROSE: Do you remember any, Dr. Ayer?

DR. AYER: No.

DR. ROSE: Some textbooks speak of mental disturbances — not unlike those seen in Korsakoff's psychosis.

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CASE 29362

PRESENTATION OF CASE

A thirty-one-year-old housewife was admitted because of jaundice of six days' duration.

Nine days before admission she developed soft, mushy, yellow, loose stools, which persisted for three or four days. Six days before entry she noticed jaundice of the skin, which became progressively deeper. Three days later she was seized with a sharp pain in the neck, both shoulders and both arms down to the elbows. The attacks lasted for fifteen minutes and left her completely exhausted. She had two similar attacks in the following two days.

She had had "arthritis and rheumatic pneumonia" at the age of twenty-one and "milk leg" at the age of twenty-seven. Two years prior to admission she developed Raynaud's disease, for which she had three hospital admissions over a period of one year. Bilateral dorsal and lumbar sympathectomies were performed with considerable relief. For the previous two years she had suffered from recurrent, slowly healing ulcers of the lower legs.

Physical examination showed a markedly jaundiced woman. The lungs were clear. There was a short systolic and a mid-diastolic murmur in the aortic area, transmitted to the neck. The extremities were warm and dry. There were many healed scars, with turgor and diminished subcutaneous tissue, on both hands.

The temperature was 99°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 3,690,000, with a hemoglobin of 10.5 gm., and a white-cell count of 12,600, with 57 per cent neutrophils. The urine had a specific gravity of 1.009, with a + test for bile and a negative test for urobilinogen; the sediment contained 4 or 5 white cells per high-power field; a culture showed many colonies of colon bacilli. The stools were guaiac negative. The blood nonprotein nitrogen was 18 mg. per 100 cc., and the van den Bergh 8.2 mg. direct, 12.3 mg. indirect. The protein was 7.6 gm. per 100 cc., the albumin being 3 gm., and the globulin 4.6 gm. — an albumin-globulin ratio of 0.7. A blood Hinton test was negative. The blood phosphorus was 2.1 mg. per 100 cc., and the phosphatase 7.9 Bodansky units. The cephalin flocculation test was ++++ in twenty-four and forty-eight hours.

The jaundice seemed to increase. On the sixth hospital day the patient had a mild chill and a slow rise of temperature to 104.5°F. about one and a half hours later, after which it fell slowly to 101.5. She became incontinent, disoriented, drowsy and restless. The breath was "mousy." There were edema and ascites. The white-cell count on the seventh hospital day was 11,400. The urine gave a ++ test for albumin and a + test for bile; it contained innumerable white cells. The patient was given daily transfusions, intravenous 25 per cent glucose and a high-vitamin and high-carbohydrate diet. One blood culture was reported positive for colon bacilli in both flasks. A blood culture taken on the next day was sterile. Giemsa stains of a blood smear failed to show any leptospira, and guinea pigs inoculated intraperitoneally with the patient's blood remained well.

On the ninth hospital day she became stuporous. The nonprotein nitrogen was 22 mg. per 100 cc., and the protein 8.6 gm. The white-cell count was 22,250. On the tenth hospital day, the temperature rose to 104.5°F. and the patient developed labored, jerky respirations with many rales and died.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN M. BRUES: This case, I think, can be described as icterus gravis or malignant jaundice.

In other words the patient had fulminating hepatic failure. This state is typified by acute yellow atrophy but may be simulated by other processes causing rapid destruction of liver tissue, notably suppurative processes. Acute yellow atrophy generally runs a course of about two weeks. It begins with mild intestinal symptoms and perhaps some fever and is thought to be catarrhal jaundice. There may be vomiting. It is interesting that this patient, so far as the record goes, did not suffer from vomiting throughout her illness. I should expect it to have occurred, and I am unable to account for its absence.

After several days in the hospital the picture suddenly became critical. This phase was ushered in by nervous symptoms, and it has been recognized for at least seventy-five years that the dividing line between benign and fatal jaundice — between catarrhal jaundice and acute yellow atrophy — is drawn by nervous or mental symptoms. These symptoms indicate "cholemia," in other words, hepatic failure. One generally sees in fulminating hepatic failure something that was not present in this patient, namely, a bleeding tendency due to a fall in the prothrombin content of the blood.

The mousy odor to the patient's breath is a subjective observation indicating that hepatic failure was being considered and that the observer thought that he had evidence for it. The patient late in the course of the disease had intermittent fever, as is seen late in hepatic failure.

Concerning the laboratory findings, the maximal cephalin flocculation test gives evidence of hepatic-cell failure. There was a very slight rise in the blood nonprotein nitrogen, which in itself is of no importance. If, when broken down, it showed a rise in the amino nitrogen and a marked fall in urea, that would be evidence of "cholemia." The plasma showed only a moderate increase in globulin, and a moderate decrease in albumin. This indicates that the process was of relatively short duration — in other words, that it did not supervene after a long course of mild hepatic failure or cirrhosis. This finding, which was made on admission, is commonly seen even in cases of simple catarrhal jaundice.

We ought to consider whether the jaundice was obstructive. I find no mention of the stools except for the observation before the onset of jaundice, when they were said to be light yellow. The phosphatase in true obstructive jaundice with relatively normal hepatic-cell function should be somewhat higher than it was here; I would expect it to go up to 10 or more units. The absence of urobilinogen suggests obstruction, — that is, failure of bile to reach the intestines, where urobilinogen is formed, — but it is well known that in acute hepatitis the urobilinogen may be absent during the acute stage and recovery heralded by its reappearance. Whether this is due to functional obstruction or to loss of function of the hepatic cells, I do not know, but I shall take the absence of urobilinogen to indicate only that the patient did not have hemolytic jaundice.

There is one secondary diagnosis that I should like to discuss at some length — a suppurative cholangitis presumably secondary to biliary obstruction. We recall that, particularly after the onset of the patient's illness, there was pain. This pain was suggestive of gallstone colic in its sudden, exhausting character. The distribution in both shoulders and the neck is not entirely characteristic of gallstone colic but is consistent with a biliary calculus. Had that pain been not quite so severe it would be easy to say that it was due to an initial swelling of the liver in the early stages of acute hepatitis. The second fact favoring cholangitis is colon-bacillus bacteremia observed on one occasion. This suggests that there was an infection, perhaps of the biliary tract, with that organism. However, it is well known that such a bacteremia may occur in the later stages of any debilitating illness, and it has indeed been mentioned as a common finding in acute yellow atrophy. Against cholangitis is the fact that fever is a prominent feature of this picture only in its late stage; the patient does not have a septic fever during the first three quarters of the illness. The differential count also shows that the neutrophils were relatively low, implying lymphocytosis. This is characteristically seen in catarrhal jaundice, and is not characteristic of a septic process.

It is obvious that Weil's disease was considered and presumably ruled out by the inability to produce disease in guinea pigs; agglutination tests with the patient's serum were not performed. In Weil's disease, as in yellow fever, we should expect more renal damage than this patient exhibited.

Another infectious process that might be considered is endocarditis, especially since the patient was thought to have rheumatic heart disease. It is improbable that endocarditis produced so much damage in the liver with no apparent damage elsewhere. Pylephlebitis entails the same objection as suppurative cholangitis, namely, that the patient was not septic during the greater part of her illness.

If we consider acute yellow atrophy the best diagnosis, we obviously ought to consider the known etiologic factors, such as the toxic effects on the liver of specific poisons. Since she was a housewife, presumably she did not work in a trinitrotoluol factory or was not exposed to other industrial hazards. There is no evidence for any other

specific poison, such as chloroform or phosphorus, that might have caused atrophy of the liver. The incidence of acute yellow atrophy is high in pregnancy; nothing in the record suggests that the patient was pregnant, but there is no definite evidence to rule it out. It has been suggested, on purely theoretical grounds, that acute yellow atrophy may be due to the regurgitation of proteolytic pancreatic juice up the bile duct; however, unless the pathologist discovered a stone in the ampulla, I hesitate to make any such diagnosis.

Before I utter a final diagnosis I should like to ask if any competent observer noted that the liver was enlarged during the terminal two or three days.

DR. WILLIAM BECKMAN: At first, it was thought to be. Toward the end no one was able to feel it.

DR. BRUES: My final diagnosis is acute yellow atrophy of the liver, to which I shall add rheumatic heart disease and probably mild aortic stenosis and regurgitation.

DR. BECKMAN: One thing not brought out in the record is that the patient pursued a very benign course during the first five days in the hospital. We thought she had catarrhal jaundice, but we were puzzled by the fact that she had no nausea or vomiting. On the fifth day she had a violent, shaking chill, and the blood culture taken at that time was the one that was positive for colon bacilli; subsequent cultures were negative. From that day on, she went downhill and was febrile.

CLINICAL DIAGNOSES

Acute hepatitis.
Septicemia (colon bacillus).

DR. BRUES'S DIAGNOSES

Acute yellow atrophy of liver.
Rheumatic heart disease (? aortic stenosis and regurgitation).

ANATOMICAL DIAGNOSES

Subacute yellow atrophy.
Acute pyelonephritis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy showed a liver that weighed about 970 gm.; the normal liver in a woman of this age and size weighs about 1500 gm. The liver was mottled yellowish purple, with slightly yellowish-green areas of apparent regeneration. Microscopic examination confirmed the marked atrophy and areas of regeneration. The atrophic regions contained an occasional single liver cell and a few remaining bile ducts. There was a fair amount of regeneration, but very little fibrosis. The process had probably been going on at least three weeks and therefore might perhaps be called subacute yellow atrophy.

The heart was small and perfectly normal. Both kidneys were enlarged and swollen and contained numerous small abscesses, which accounted for the colon-bacillus septicemia and certainly must have been an added burden to a patient with severe liver insufficiency. The biliary tract was normal; there were no stones or dilation of the bile ducts.

DR. WILLIAM B. BREED: What was the sequence in this case? Did the kidney infection and the septicemia precipitate the liver disease? What was the etiology of the acute yellow atrophy?

DR. CASTLEMAN: I cannot explain the sequence in this case. It is believed that catarrhal jaundice and acute yellow atrophy may have the same etiology. Thus, if the patient with jaundice, due perhaps to some infection, gets well it is called catarrhal jaundice; if the patient dies, it is called acute yellow atrophy. Several years ago during an epidemic of catarrhal jaundice in Sweden, the incidence of acute yellow atrophy was also increased.* Most of the cases of acute yellow atrophy that we have seen have been due to drugs, such as arsphenamine and cinchophen-containing products.

*Bergstrand, H. *Über die akute und chronische gelbe Leberatrophie mit besonderer Berücksichtigung ihres epidemischen Auftretens in Schweden im Jahre 1927.* 114 pp. Leipzig: Georg Thieme, 1930.

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GRADUATE TEACHING SERVICE FOR THE ARMY, NAVY AND COAST GUARD

THE past summer witnessed the formation of the New England Committee for Wartime Graduate Medical Meetings. This represents the combined efforts of the New England state medical societies, including the Military Postgraduate Committee of the Massachusetts Medical Society, and the National Committee for Wartime Graduate Medical Meetings, sponsored by the American Medical Association, the American College of Physicians and the American College of Surgeons.

Three types of graduate medical instruction are offered to the Army, Navy and Coast Guard: the usual medical meeting, with the program lasting one or two hours and covering a specific subject; a longer meeting, lasting through an afternoon and evening, with a program on one or more related subjects by several speakers, and including both clinical and didactic instruction; and a three-day program, which covers any desired field of medicine and consists of lectures, demonstrations, ward rounds and panel discussions. Application for either of the first two types of instruction is made through the office of the committee at the headquarters of the Massachusetts Medical Society; however, requests for the more comprehensive program must be taken up through the official service headquarters — the First Service Command, the First Naval District or the district office of the Coast Guard. Although instruction for service installations with relatively few medical officers will be given whenever possible, it is hoped that such groups will be able to attend meetings at the larger nearby organizations.

Notices regarding these opportunities for postgraduate instruction and application forms have been forwarded to all service installations in New England. Many requests have already been received, and the first meeting was held at the Station Hospital, Fort Devens, on September 7. It is apparent that medical officers appreciate what is being offered, and those who have given and are giving so much of their time and effort to the organization and continuation of these facilities deserve great credit.

ENGLAND AS A HEALTH RESORT

AN article published in the March issue of the *Statistical Bulletin* of the Metropolitan Life Insurance Company reveals the amazing but encouraging fact that England's death rate in 1942, her third year of total war, had declined, with substantial improvements in practically every important disease. In addition to this lowered death rate the birth rate was apparently the highest since 1930 or 1931, the number of babies born ex-

ceeding 650,000 for the first time since 1928. Moreover, the proportion of stillbirths to total births declined in the third quarter of the year to the lowest level on record, and the infant mortality approached the record low level of 50 per 1000 live births established in 1939.

These figures are not compatible with nation-wide malnutrition, nor would they be found in a nation facing defeat after more than two years of war. They reflect rather, as the bulletin phrases it, the inspiring resilience of England's people under stress.

In general, despite wartime conditions and air-raid casualties, the death rate in England last year was restored to its prewar level. Epidemic meningitis, always a war disease, markedly increased after the outbreak of hostilities; in 1942 its morbidity fell to about half that of 1940-1941, with, of course, under modern methods of treatment, an extremely low mortality rate. Tuberculosis, which had increased sharply in 1940 and 1941, showed a much lower incidence, the improvement being most noticeable among women and children. Deaths from diarrhea and enteritis among infants and young children increased slightly over the rate prevailing in 1941, but the deaths from diphtheria fell off sharply and epidemic respiratory diseases were conspicuous by their absence. Deaths from diabetes dropped, — overeating has not been an outstanding fault in England in the last three years, — and the mortality from peptic ulcer showed a sharp decline, furnishing as fine a bit of evidence as could be found that the emotional stress of recent years has been relieved. The suicide rate was lower, further illustrating the fact that men rarely despair of life when they have a job in hand, and the air-raid deaths continued their decline from the dreadful month of September, 1940, when nearly 7000 civilians were killed. Even fatal road accidents, which have been a black mark on the escutcheon, declined 24 per cent last year from the peak of 1941.

These conditions may not continue, and the middle two of the famous horsemen may again ride with their flanking companions, but at least for the present, it can be said that a superb job of adjustment to war conditions has been done and that thumbs are still up in Merry England.

MEDICAL EPONYM

Cushing's Disease

Dr. Harvey Cushing (1869–1939), professor of surgery at Harvard Medical School, first described this disease in a paper entitled "The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations (Pituitary Basophilism)," which appeared in the *Bulletin of the Johns Hopkins Hospital* (**50:** 137–195, 1932). After discussing 12 cases he concludes:

> . . . A polyglandular syndrome hitherto supposed to be of corticoadrenal origin characterized in its full-blown state by acute plethoric adiposity, by genital dystrophy, by osteoporosis, by vascular hypertension, and so on, has been found at autopsy in six out of eight instances to be associated with a pituitary adenoma which in the three most carefully studied cases (Cases 6, 7, 10) has been definitely shown to be composed of basophilic elements, the lesion in one instance (Case 7) having been clinically predicted before its postmortal verification.
>
> While there is every reason to concede, therefore, that a disorder of somewhat similar aspect may occur in association with pineal, with gonadal or with adrenal tumors, the fact that the peculiar polyglandular syndrome, which pains have been taken herein conservatively to describe, may accompany a basophil adenoma in the absence of any apparent alteration in the adrenal cortex other than a possible secondary hyperplasia will give pathologists reason in the future more carefully to scrutinize the anterior-pituitary for lesions of similar composition.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council of the Massachusetts Medical Society will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 6, 1943, at 10:00 a.m.

Business:

1. Call to order at **10:00 a.m.***
2. Presentation of record of meeting held May 24, 1943. (Published in the *New England Journal of Medicine*, issue of July 8, 1943.)
3. Reports of standing and special committees.
4. Appointment of an auditing committee.
5. Fill any vacancies in the offices of the Society.
6. Such other business as may lawfully come before this meeting.

Michael A. Tighe, M.D., *Secretary*

*It should be noted that the meeting will be called to order at 10:00 a.m., rather than at 10:30 a.m.

ADVANCE INFORMATION FOR THE COUNCIL

Report of Progress by the Postwar Loan Fund Committee

The Postwar Loan Fund Committee was organized on June 16, 1943, with fifteen members appointed by the president, Dr. Roger I. Lee.

The second meeting of the committee of the whole was held on Wednesday, August 11, 1943, at 8 Fenway, Boston, at which time the reports of the five subcommittees appointed by the chairman to study certain phases of this problem were read by the chairman of each subcommittee and discussed by all members of the committee of the whole. This is a report of progress of the committee of the whole.

The first subcommittee (Dr. Peirce H. Leavitt, chairman) studied the following questions:

(1) Amount of loan to be granted.
(2) Whether or not interest is to be charged.
(3) Whether or not endorsers will be necessary.
(4) Length of time the loan may run.

The committee reported that it believes that the amount must, of course, be uncertain, but would depend on two factors: the amount of money raised by the Society and the need of the applicant. The committee expressed the opinion that just enough interest to remind the applicant that he had a loan and to cover the carrying charge should be collected — this interest not to exceed 2 per cent. The committee stated that in its opinion no endorsers should be asked from members of the Society, and further stated that the length of time the loan may run should be within a two-year period. The committee of the whole, after discussing this subcommittee's report, accepted these conclusions.

The second subcommittee (Dr. Walter G. Phippen, chairman) then reported on the questions studied by them:

(1) Eligibility of persons to borrow money from the fund.
(2) Whether or not physicians other than members of the Massachusetts Medical Society at the time of entering the armed services should be permitted to borrow from the fund.

The committee reported that it believed that only men who were members of the Massachusetts Medical Society when they entered the armed forces should be permitted to borrow from the fund. None of the members believed that the fund should be open to all physicians in Massachusetts. The committee of the whole discussed this report, and it was approved in principle.

The third subcommittee (Dr. Charles Wilinsky, chairman) considered the question whether the fund should be raised by:

(1) Increasing dues.
(2) Assessing members $10 or more for one year.
(3) Assessing members $10 or more over a period of three to five years.

The committee reported as follows:

> It is our considered opinion that these funds should be raised not by increasing the dues, but rather by an annual assessment of $10 for the duration of the war, unless otherwise modified by future action of the Council.

The committee reported that the present by-laws of the Society make provision for such assessments and authorize the Treasurer to collect them. The report of this subcommittee was considered at great length by the committee of the whole, and the report was accepted in principle.

The fourth subcommittee (Dr. Herbert L. Lombard, chairman) reported on how best to inform the members of the Society in the armed forces of the availability of this fund. The committee reported as follows:

> We unanimously agree on three points:
>
> Information should be printed in the *New England Journal of Medicine*. There should also appear in a box on the cover of the *Journal* an announcement calling the article on the inside page to the attention of members.
>
> Form letters should be sent to men in the armed services notifying them of this action by the Society.
>
> Form letters should be sent to other members of the Society with the annual bills for dues, stating the availability of these loans.

This report was also accepted in principle by the committee of the whole after considerable discussion.

The fifth subcommittee (Dr. George Leonard Schadt, chairman) made a report on the question concerning the relation of the individual county district societies to the Society in developing and making the Postwar Loan Fund workable. The subcommittee believed that the fund should be administered from the headquarters of the Massachusetts Medical Society, rather than from the district societies, so that no member would be embarrassed in going to his district society and asking for a loan. It was also thought that a member desiring a loan would be more apt to ask for it if it were done through the headquarters of the Society. This question was also discussed at length and agreed to in principle by the committee of the whole.

George Leonard Schadt, *Chairman*

Report of the Committee on Public Relations

Congress has appropriated funds to provide medical, nursing and hospital maternity and infant care for wives and infants of enlisted men up to the seventh pay grade under plans developed and administered by state health agencies and approved by the chief of the Children's Bureau.

The Committee on Public Relations met in conference with Dr. Vlado A. Getting, state commissioner of public health, who discussed the administration of this plan in Massachusetts. In this state all deliveries will be in a hospital. All deliveries will be by graduates of Grade A schools or by those approved by a technical committee; the latter committee for the most part is identical with the Committee on Maternal Welfare of the Massachusetts Medical Society. Dr. Getting in this connection pointed out that a ruling by the Attorney General of the Commonwealth made it possible for the Department of Public Health to set standards for the care of the patients coming under this provision that are

different from those set by the Board of Registration in Medicine. In other words, the right to practice medicine in Massachusetts does not necessarily give the individual doctor the right to participate in this plan.

The service in Massachusetts will be limited to the wives and offspring of privates and the next three higher grades of enlisted personnel of the Army, Navy and Marines. The application for help, under this plan, must be signed by both the physician and patient.

The plan provides for the payment for consultations with other obstetricians, pediatricians and surgeons. These services are to be paid for without deduction from the sum agreed on in the original plan for obstetric care. The maternity benefit is limited to those who are willing to accept ward care in a hospital. The doctor is to be paid the sum of $50 for the prenatal, the delivery and ordinary post-partum care. Home visits are to be paid for at the rate of $5 to $10 for the first visit and lower fees for subsequent visits.

Hospitals within Metropolitan Boston are to be paid at the rate of $4.50 a day, and those outside of this area at the rate of $3.50 a day.

Dr. Getting asked for the endorsement of this plan in principle only. The Committee on Public Relations endorses the plan in principle.*

Further information on this subject is contained on page 945 of the July 31, 1943, issue of the *Journal of the American Medical Association.*

ALBERT A. HORNOR, *Secretary*

DEATHS

BRENNAN — JOHN J. BRENNAN, M.D., of Worcester, died August 26. He was in his eightieth year.

Dr. Brennan received his degree from Harvard Medical School in 1886, and later studied in Vienna and London. He was a member of the Massachusetts Medical Society and the American Medical Association and a former member of the State Board of Optometry.

His widow, two sons and a daughter survive.

DAUDELIN — S. ALPHONSE DAUDELIN, M.D., of Worcester, died August 28. He was in his seventy-fourth year.

Born in Sutton, P. Q., Dr. Daudelin received his degree from Laval University, Montreal, in 1895. He was one of the original founders of the old Franco-American Dispensary, which was the parent of the former Louis Pasteur Hospital. In 1907, Dr. Daudelin was appointed by President Theodore Roosevelt as high commissioner and plenipotentiary from the United States to France for a period of six months covering the Maritime Exposition. The French government awarded him the Cross of Knight of the Legion of Honor, and on the completion of his mission, Dr. Daudelin remained in France for advanced study, specializing in eye, ear, nose and throat. He was elected to membership in several important French medical societies, and was named and served as head of the eye and ear clinic at Amiens, France. While in Paris, Dr. Daudelin helped found the Comité France–Amérique, an organization that now has branches in all leading cities in this country. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives.

*The Executive Committee at its meeting on August 25, 1943, likewise endorsed the report in principle.

MISCELLANY

NOTE

Dr. Harry C. Solomon has recently been appointed professor of psychiatry at Harvard Medical School and medical director of the Boston Psychopathic Hospital. He succeeds the late Dr. C. Macfie Campbell.

AWARD TO GENERAL ELECTRIC X-RAY CORPORATION

Robert P. Patterson, Under Secretary of War, has recently announced a second award for excellence of war production to the General Electric X-Ray Corporation, of Chicago. This permits the company to add a white star to its Army–Navy "E" flag, which has flown over the plant since January 26 of this year.

BOOK REVIEWS

A Short History of Cardiology. By James B. Herrick, M.D. 8°, cloth, 258 pp., with 48 plates and frontispiece. Springfield, Illinois: Charles C Thomas, 1942. $3.50.

In this interesting résumé of the history of cardiology, Herrick first reviews the period from Hippocrates to Harvey, and rightly calls attention to the fact that in the Hippocratic writings, although there is an interesting fragment on the anatomy of the heart, the only consideration of its function is the employment of the pulse in the estimation of fever, whereas the matter of the pathology is scantily treated, in fact was practically unknown. Aristotle's mistake in attributing to the heart the functions of the brain is well known. Celsus was responsible for the confusion of disease of the heart with that of the cardiac opening of the stomach, the *morbus cardiacus*, which produced so much confusion for so many years.

The great Galen knew the anatomy of the heart, except for his fatal mistake about the pores in the septum, which kept him so far from the true explanation of circulation. Nonetheless, eminent authorities have said that he contributed more to our knowledge of the heart than anyone before Harvey. He proved by experiment that the arteries contained blood and not air, and the acuteness of his observations is shown by his discovery in the embryo of the ductus arantii and ductus botalli, of which, however, he had no conception of the function. He gave tremendous and even bewildering attention to the pulse, writing sixteen essays on that subject.

The author gives an interesting résumé of progress of knowledge of cardiology during the two hundred years preceding Harvey and rightly calls attention to the influence of important world events, such as the invention of printing and gunpowder, the fall of Constantinople and the discovery of America, on medicine in general and on cardiology in particular.

Leonardo da Vinci's influence on cardiology is adequately treated, and a drawing of his is reproduced that shows even the moderator bond of the right heart. The contributions of Vesalius and the martyr Michael Servetus are well described. The next period includes Harvey to Laennec. The author truly says that no abstract of Harvey's work can do it justice. The story of the contributions and controversies of Columbus and Fabricius are well told. Facts about Lower, Mayow and Hales bring out the fascinating story of the gradual growth of knowledge by the scattered contributions of individuals.

Space does not allow details regarding the progress of

the story of cardiology down to present times; the parts played by all the great contributors are taken up in order and adequately discussed in a masterly fashion. The book throughout is characterized by a broad point of view. It is extremely well illustrated, with portraits of the principal participants in the march of science. The book is fascinating reading, and to him who seeks — and who does not — the history of an important part of medical knowledge, it can be most highly recommended.

Manual of Oxygen Therapy Techniques, including Carbon Dioxide, Helium and Water Vapor. By Albert H. Andrews, Jr., M.D. 12°, cloth, 191 pp., with 33 figures and 16 tables. Chicago: The Year Book Publishers, Incorporated, 1943. $1.75.

This is a technical handbook rather than a medical textbook on gas therapy. Accordingly, only a little over four pages are given to the medical aspect of this subject. In the chapter entitled "Physiology of Respiration and Rationale of Inhalation Therapy," the author manages to clarify the mechanism of respiration in terms of ventilation, the transportation and absorption of oxygen, and the elimination of carbon dioxide. From an adequate oxygen supply, which is derived from normal breathing, the author passes over to the abnormal condition in which anoxia or "oxygen want" occurs. To relieve this oxygen deficiency, he suggests the use of gas therapy, employing oxygen, carbon dioxide, helium and water vapor.

The rest of the book is strictly technical and is therefore crowded with details, tables and figures. These relate to the purchase and maintenance of equipment from the standpoint of economy and efficiency, as well as the indications for use, the technic of application and the necessary precautions. In addition to the usual procedures, the author pays attention to certain exceptional cases. Thus, he gives specific instructions for this form of treatment when it is administered to infants in incubators or when it is to be carried out in the home, where hospital facilities are lacking.

The reviewer is not aware of the existence of an oversupply of texts on this subject. He is therefore of the opinion that this manual will prove to be a useful guide to those of the medical profession who are called on to administer gas therapy.

The Principles and Practice of Medicine: Originally written by Sir William Osler. By Henry A. Christian, M.D., LL.D., Sc.D. (hon.), F.R.C.P. (Can.). Fourteenth semicentennial edition. 4°, cloth, 1475 pp. New York: D. Appleton-Century Company, Incorporated, 1942. $9.50.

There is something appealing about meeting a book that is fifty years old and still young, that has gone through fourteen editions, each one successful, and that has kept alive a tradition of good medical writing through the hands of three different authors.

The fourteenth edition of Osler looks not unlike the first: the reviewer's copy of the first edition happens to be bound in green whereas the fourteenth is in red. But the two books can stand side by side companionably, as should all medical fathers and sons, the older book perhaps still able to show the younger something in the way of literary style. Youth in return now adds to the parent volume a full half century of new ideas, customs and medical knowledge.

When Dr. Christian took over the task of editing the thirteenth edition of Osler he did this with a sympathetic understanding of what Osler had in mind. This edition appeared in 1938 and was at once well received by the medical reading public. That it was successful is proved by the fact that a new edition has been forthcoming so quickly.

The fourteenth edition begins with a chapter on functional diseases of the nervous system, an arrangement that might have made Dr. Osler smile. The book continues to be a complete handbook of internal medicine, up to date in every particular and continuing to have what, to the reviewer at least, is a particular charm — the even character of writing that can be found only in a one-man book. Each chapter has now appended a select group of references to important literature. Tropical diseases are discussed in a way that will appeal to all medical officers. On the whole, any student or practicing physician brought up with an admiration for Osler will feel that this textbook is still the proper one to use.

Clinical Anesthesia: A manual of clinical anesthesiology. By John S. Lundy, M.D. 8°, cloth, 771 pp., with 266 illustrations. Philadelphia and London: W. B. Saunders Company, 1942. $9.00.

Dr. Lundy has contributed his wide experiences of over twenty-five years in the practice of anesthesia. They are mostly personal expressions gained at the Mayo Clinic. There is much controversial material in the book; however, the author is frank and honest in his statements, which are fortified by an experience probably unequaled by any anesthetist in the country.

Dr. Lundy deserves much credit for pioneering in the field of anesthesia, having established the use of many of the newer drugs and technics, and many of the procedures described in his book were originated by him. In the opinion of the reviewer, reference to the works and technics of contemporaries and mention of the variety of apparatus and equipment in universal use, together with more illustrations, would have given the reader a broader knowledge of modern anesthesia.

The book opens rather abruptly with the choice of anesthetic agents and methods. If the reader were introduced to the basic fundamentals of anesthesia and if the development of the subject matter followed in chronological sequence, it seems that a clear picture of anesthesia as a whole would be presented. The tabulation of anesthetic agents and methods according to the various surgical procedures is unique; comments in the text are referred to by interrogation points on the charts.

The following chapter, covering the use of local anesthetic agents, is well written and extremely valuable. It is the high light of the book for reference by anesthiologists and surgeons.

The chapter on spinal anesthesia relates the author's personal experiences but does not enlighten the reader concerning the many advances made with agents other than procaine. More emphasis on this subject would have aided the reader. The author's opinions on complications and dosages are stressed.

The chapter on equipment and drugs is extremely well written with many suggestions of value.

The next seven chapters consider general anesthesia, the stages and signs of general anesthesia, preoperative and postoperative care, the agents employed for general anesthesia and the gaseous agents used for the support of respiratory function. It seems as though more refer-

ence could have been given to the technic of carbon dioxide absorption, which has revolutionized the administration of inhalation agents.

Endotracheal or intratracheal anesthesia is well described, as well as its many complications.

The chapter on general anesthesia in dentistry and obstetrics barely covers two important fields of surgery that have been sadly neglected.

The chapter on intravenous anesthesia is excellent, as might be expected, since the author has been responsible for pioneer work in this field. The methods of rectal and oral instillation rate the few pages consistent with their position in anesthesia. Balanced anesthesia, a term coined by the author, is mentioned in a two-paragraph chapter.

The chapter on anesthesia for nonsurgical conditions demonstrates the mastery of the author in diagnostic, prognostic and therapeutic nerve blocks, procedures concerning which most physicians are relatively ignorant.

The remaining chapters and the appendix cover venipuncture, intravenous therapy, resuscitation, records, the anesthetic statistics of the Mayo Clinic from 1924 to 1940, and the chemistry of analgesics and anesthetics, as well as a chronological table of anesthesiology and allied subjects and conversion tables of weights and measures.

This book is well worth reading for reference to the experiences, impressions, and recollections of a pioneer physician and master in modern anesthesia.

Diseases of the Liver, Gallbladder and Bile Ducts. By S. S. Lichtman, M.D. 8°, cloth, 906 pp., with 122 illustrations and 1 colored plate. Philadelphia: Lea and Febiger, 1942. $11.00.

This book is a great storehouse of facts and opinions about the liver and its diseases. Its value is increased by a long list of well-chosen references at the end of each chapter. The material is so varied and extensive that it is hard to single out special chapters for review.

The book is well arranged, starting with 100 pages on the structure and physiology of the liver, followed by about 50 pages on liver poisons, nutrition, diet in protection and damage to the liver, the role of vitamins, and the mechanism of jaundice. In discussing jaundice, only Rich's classification into retention and regurgitation types is described. From the reviewer's point of view, McNee's classification of external obstructive, hepatocellular and hemolytic jaundice seems more useful.

About 50 pages are given to the symptomatology of diseases of the liver; the section is well arranged, although the description of the various symptoms and signs is somewhat uneven in quality. Regarding the spleen, the practicing physician is probably more interested in the percentage that are palpable than that of those weighing more than 300 or 600 gm. at necropsy.

About 95 pages are devoted to a description of laboratory aids and liver-function tests, all of which is valuable for reference. Many of the fifty tests described are little used now and have only a historical interest. The inclusion of so many tests is possibly confusing to the practitioner.

Then follow about 400 pages covering specific diseases of the liver. The author's classification of seven types of catarrhal jaundice seems rather elaborate in a disease in which necropsy is rare, and their separation into two groups — with and without initial gastrointestinal symptoms — appears to be somewhat artificial. Cirrhosis of the liver is given an especially complete description. To list ten types of cirrhosis on one page is rather confusing, but this disease is described under the familiar headings — portal, biliary and pigment cirrhoses and Banti's disease. In the jaundice of hepatocellular disease (catarrhal jaundice, toxic hepatitis, cirrhoses and so forth), the author seems to overemphasize the mechanical factor of obstruction within the liver and to minimize the poor excretion of bilirubin by the damaged lobular cells. The chapter on the hepatorenal syndrome does not help much in clarifying this difficult subject. The figures for the incidence of syphilis of the liver date back to a generation or two ago, when the diagnosis and treatment of syphilis were very different from what they are at present; it is now a relatively rare disease in the ward or at necropsy. The incidences of the common types of jaundice, differential diagnosis and diagnostic errors are given careful consideration.

In addition to the paragraphs on treatment under the various diseases, a 25-page chapter is given to the treatment of liver disease in general; this is sound and up to date, but might well be enlarged at the expense of the many pages on laboratory procedures.

The last 110 pages are devoted to diseases of the gall bladder and biliary passages.

The author has drawn liberally on the best literature for facts, opinions, tables and illustrations. The paper, type and illustrations are excellent, as are many of the photomicrographs.

Nasal Medication: A practical guide. By Noah D. Fabricant, M.D. 8°, cloth, 122 pp., with 20 illustrations. Baltimore: The Williams & Wilkins Company, 1942. $2.50.

This book is a practical guide not only for the specialist in rhinology but also for the general practitioner and pediatrician. The author is associate in laryngology, rhinology and otology at the University of Illinois College of Medicine. He has devoted considerable time to research in the physiology of the nasal mucous membranes and in the pharmacologic action of the common drugs used in nasal medication. The book includes a brief section covering the anatomy of the nasal cavity and the paranasal sinuses, including both gross anatomy and histology. He also discusses histopathology and nasal physiology. In the latter subject, the biochemistry of the nasal secretions is discussed and the hydrogen ion concentration of these secretions is described in considerable detail. The significance of the latter has only recently been recognized, and the author is one of the most enthusiastic contributors to this newer conception of nasal physiology. A great deal of emphasis is laid on the effect of drugs on ciliary action, it being considered particularly harmful to destroy or inhibit this action, which is of tremendous importance in keeping the nasal mucous membrane free of foreign particles.

Contrary to common belief, menthol, camphor and eucalyptol seem to have no beneficial effect in opening the nasal passages, in fact menthol in some experiments has seemed to produce a narrowing of the nasal passages and an increase in the resistance to the stream of air passing through the nose. The cooling action of menthol has probably caused patients to believe that there was a clearing of the airway. The author adds, "Definite destructive changes throughout all layers of mucous membrane are produced by a 5 per cent solution of menthol."

Ephedrine hydrochloride seemed to produce little if any change in the tissue, whereas epinephrine hydrochloride in dilutions of 1:1000 used over a long period of time caused considerable damage to the tissues.

It is recommended that, if aqueous solutions are used, they should be isotonic. There is a discussion of the use of oils as sprays or drops, including the possible complication of lipid pneumonia. A great deal has been written by many authors on the latter subject. This author summarizes the pros and cons. He quotes Wishart, who points out that there are really very few cases of lipid pneumonia when one considers the large amount of oil inhaled by an enormous number of people.

There are short discussions on the use of silver nitrate, zinc ionization, sodium sulfathiazole and Mercurochrome.

Finally, there is a complete description of methods of applying nasal medication. These include the displacement method of Proetz, the lateral-head low-posture method, Beck posture, nasal tampons, sprays, cotton applicators, inhalers, jellies and emulsions, irrigations and even snuffs. Irrigation of the sinuses is also discussed, and at the end there is a chapter on nasal medication in disease.

The book is clearly written. It is not too technical and is well documented. It gives a fair discussion of many controversial subjects. Its greatest value is a real attempt to place nasal medication on a scientific basis.

The Electron Microscope. By E. F. Burton, Ph.D., head of the Department of Physics and director of the McLennan Laboratory, University of Toronto; and W. H. Kohl, development engineer, Rogers Radio Tubes, Limited, Toronto. 8°, cloth, 233 pp., with 144 illustrations. New York: Reinhold Publishing Corporation, 1942. $3.85.

No library should be without this extremely valuable book. The electron microscope is destined to play an increasingly important part in the newer experimental technics that are to be applied in the field of biology, of which medicine is integral. The authors are to be congratulated on the readable style of their book. There are many instructive diagrams and plates, and a useful general bibliography is appended.

Contribucion al estudio anatomo-clinico de las affecciones del endocardio. A doctorate thesis (Universidad Nacional de Buenos Aires, Facultad de Ciencias Medicas, No. 5636) by Manual Perea Muñoz. 4°, paper, 363 pp., with 92 illustrations. Buenos Aires: "Esmeralda," 1942.

This thesis is simultaneously a brief review of the literature on endocarditis and an analysis of 206 cases of abnormalities of the endocardium in a series of 1000 autopsied cases studied since 1936 in the Laboratory of Pathological Anatomy, Ramos Mejia Hospital, Buenos Aires. Among these cases, there were 64 with valvular disease.

The twenty-five chapters in the book take up the classification of endocarditis and discuss acute and subacute bacterial endocarditis, syphilitic involvement of the endocardium, rheumatic endocarditis, "benign" endocarditis, endocardial atheroma and calcification, neoplastic disease and malformations, along with valvular defects.

The author's 206 cases are summarized under the headings of the various chapters. Of 44 cases of bacterial endocarditis, 15 are said to have been the result of sepsis, 4 are labeled terminal, 5 acute bacterial, and 20 subacute bacterial. Fifty-four cases on a rheumatic basis are also summarized, 36 in men and 18 in women. Thirteen cases of syphilitic involvement of the endocardium are included, as well as 41 cases of atheroma of the endocardium and 27 of valvular sclerosis. A few congenital defects are also added, but they can hardly be classed as true endocardial disease.

The volume presents detailed studies of this rather small group of cases, but the lesions are so varied and the cases in the different categories are so few that statistically the volume is of little importance and it seems larger than necessary for presentation of these data. The chief value of the book lies in the individual case reports, which are worthy of perusal. The volu.ne is well printed and the illustrations are good. There is a short bibliography.

Effects of Alcohol on the Individual: A critical exposition of present knowledge. Volume 1. *Alcohol Addiction and Chronic Alcoholism.* Edited on behalf of the Scientific Committee of the Research Council on Problems of Alcohol by E. M. Jellinek, Sc.D. 8°, cloth, 336 pp., with 43 tables and 5 figures. New Haven: Yale University Press, 1942. $4.00.

The Research Council on Problems of Alcohol, a recent organization, has been extremely active. Under the chairmanship of Dr. Karl M. Bowman, and with a board of men, most interested in this problem, it has fostered research and issued an excellent journal, *The Quarterly Journal of Studies on Alcohol*, from the Laboratory of Applied Physiology, Yale University.

This book is a survey of the general problems, with extensive bibliographies. The book is divided into sections on alcoholic addiction, mental disorders associated with alcoholism, studies on vitamin deficiencies, the encephalopathics, cirrhosis of the liver and Marchiafava's disease. In these finely written chapters, one has at hand an up-to-date account of each subject, thoroughly documented, with the literature carefully analyzed. Much of this literature, incidentally, was collected by Dr. Merrill Moore, under the direction of the Works Progress Administration.

The book can be highly recommended as a comprehensive review of the subject, as a reference work and as a basis for studies on an acute problem, particularly important in wartime.

Surgical Physiology. By Joseph Nash, M.D. 4°, cloth, 496 pp., with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1942. $4.00.

This book is based on lectures given by the author at New York University College of Medicine as part of a graduate course in surgery. As indicated by the title, aspects of physiology that are of especial importance in surgery have been emphasized. The text is written in a clear, concise manner. The book is divided into seven sections dealing with the following subjects: the circulatory system, the respiratory system, the alimentary system, the body fluids, the endocrine glands, the cerebrospinal nervous system and the autonomic nervous system. There is an excellent list of references dealing essentially with the more recent contributions of physiology to surgery.

This book should make a strong appeal to the practicing surgeon and to the postgraduate student.

(Notices on page xii)